DRUG RESISTANCE and CHEMOTHERAPY OF MALARIA IN INDIA

AN UPDATE DECEMBER 1997

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PREFACE

Malaria is one of the major public health problems of the country. Although with the effective implementation of National Malaria Eradication Programme in 1958 and its revised version i.e. Modified Plan of Operation (MPO) since 1977, annual incidence of malaria has been brought down from estimated 75 million cases to about 2 million cases per annum but the proportion of *Plasmodium falciparum* cases has increased from 15% to 40% in the country, during last three decades. The problem is mainly confined to the hard core, hilly and forested areas, predominantly inhabited by tribal populations. The emerging problem of resistance of *P. falciparum* to chloroquine, the most commonly and widely used antimalarial, has further precipitated malaria problem in the country.

The *P.falciparum* species is spreading wider as the migration of population from endemic to non-endemic areas and vis-a-vis has increased tremendously. This is a serious concern of the programme as this species is responsible for malaria mortality. All the efforts are to be made to contain the spread of this species.

The first resistant focus of *P.falciparum* to chloroquine was reported from Assam in 1973. Subsequently the resistant problem spread to the entire north-east followed by other states in the country. The drug monitoring teams under the NMEP have been established since 1978 and are at various Regional Offices of Health and Family Welfare , for systematic monitoring of drug resistance in *P.falciparum*, in different states of the country.

These teams have been conducting drug sensitivity tests in *P.falciparum* cases whenever and whereever clinical observations of resistance to chloroquine is reported by state health authorities and also some attempts have been made to undertake such studies to alternate antimalarials i.e. sulfa pyrimethamine also by undertaking trials on alternate antimalarial drugs. Based on the reports of these teams the drug policy for the these areas is decided and if needed a second line of drug i.e. Sulfa Pyremethamine combination is switched over for the effective control of *P.falciparum* cases.

Proper implementation of drug policy, effective operational activities of the programme and education of the community may avert the emergence of drug resistance problem. Further proper deployment of antimalarials and prevention of misuse of second and third line of antimalarials is the most important factor for avoiding untimely development of drug resistance to other drugs. The special focus on vulnerable areas is essential. In view of non-availability of an effective malaria vaccine, early detection and prompt treatment, effective implementation of drug policy and judicious use of appropriate insecticides for vector control are the most important public health approaches for effective malaria control.

I feel that this document shall prove to be an useful reference document to all concerned health professional, especially those involved in malaria control. The comments and suggestions from readers shall be appreciated as that will guide us for further improvement of this document

Delhi
March 1998

(Shiv Lal)

ACKNOWLEDGEMENTS

This document "Drug Resistance and Chemotherapy of Malaria in India, an update December - 1997 " has been prepared for the reference of all those involved in the control of malaria in the country. An attempt has been made to give an updated information on drug resistance and the current chemotherapy policy of NMEP. However, it is relevant to mention here that in view of the wide emerging drug resistance problem , all the states should come forward to build up their own capacities for carrying out drug sensitivity studies which was olne of the recommendation of expert committee of chemotherapy of malaria 1995. Preparation of this document was a team effort and all the concerned sections of the Dte. of NMEP have contributed to accomplish this task for which we are thankful to the officers and staff of NMEP.

Dr. P.K.Phukan, Additional Director, NMEP, has readily provided administrative support for the preparation of this document. We are grateful to him and extend our sincere thanks to him for his kind help.

This document is based on the information gathered from the P.falciparum monitoring teams of NMEP deployed at Regional Offices for Health and Family Welfare in various states. Without their help it would have not been possible to commence the task . We express our gratitude to all the officers and staff of these teams.

A previous status report "Drug Resistance Status of P. falciparum in India (Situation Analysis)" compiled by Dr.S.P.Mishra, Dr.B.Sita Rama .Rao and Dr.Neeraj Dhingra, has been used as a base document for producing this document. We are extremely thankful to the authors as this has saved lot of time and energy.

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Delhi

March 1998

(G.P.S.Dhillon)
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EXECUTIVE SUMMARY

For the effective control of malaria national level effort has been made since 1953 when National Malaria Control Programme (NMCP) was launched. The spectacular results achieved by NMCP led to launching of National Malaria Eradication Programme (NMEP) in the year 1958. The main thrust was only on the vector control with DDT spray. The incidence of malaria was brought down to as low as 0.1 million cases annually in the year 1965.. Subsequently due to various reasons including vector resistance to the insecticides, there was upsurge in the malaria incidence and cases rose up to 6.47 million annually in the year of 1976. This rise in incidence of malaria necessitated the review of programme and a Modified Plan of Operation (MPO) was launched in 1977. Incidence of malaria was brought down to 2.18 million cases annually by the year 1984 . Thereafter the malaria situation was static for about a decade till 1993. Since 1994 the focal outbreaks have been reported from various parts of the country. The proportion of P.falciparum is increasing for the last more than a decade. At present the main thrust of the programme is given on the early case detection and prompt treatment. Thirteen P.falciparum monitoring teams of NMEP have been constituted and deployed at the Regional Office for Health & Family Welfare in various states. The present document has been prepared to give a view on drug resistance, methodology of monitoring of resistance, the status of resistance in the country, states as well as at the district level as to appraise the concerned health authorities for taking appropriate containment measures.

Chemotherapy: Chemotherapy is one of the most important aspects of malaria control programme. In view of emerging resistance problem of P.falciparum cases which is a malignant variety of malaria known to cause mortality, an appropriate chemotherapy has become an essence of effective control of malaria. In the year of 1995 an Expert Committee on chemotherapy was constituted by the Govt. of India to look into every aspect of chemotherapy of malaria and to formulate an appropriate drug policy for the country. Proper deployment of antimalarials is very important not only for control of malaria but also to avoid untimely development of drug resistance.

Emergence of Drug resistance: During last few years the malaria mortality has gone up. One of the contributory factors is attributed to resistance of P. falciparum to chloroquine. The chloroquine resistance was first detected in 1973 in the State of Assam since then many resistance foci have been detected in the various parts of the country. The sporadic cases of resistance in P.falciparum to other antimalarials like Sulfa–pyremethamine combination are also being detected .The timely and adequate treatment of malaria cases with antimalarial drugs is the most important approach to avert development of resistance.

Drug resistance of India: Since 1978 the P.falciparum monitoring teams have been working in various parts of the country to detect the P.falciparum resistance to

chloroquine and other antimalarials. It has been observed that as the proportion of Pf. cases to total malaria cases is increasing, the resistance level of RII & RIII are being detected in high proportion. Till 1997 sensitivity tests were conducted in 12863 cases of which 3065 were found to be having various levels of resistance. There are 278 resistance foci distributed in 26 states and U.Ts. The second line of drug i.e. sulfa-pyremethamine combination is being used for the treatment of P.falciparum cases in some areas of 12 districts of 9 states /U.Ts. in the country. Further some areas of 8 districts of 6 States /U.Ts, have been identified for introduction of the alternative antimalarial .

The key for effective control of malaria is early detection and prompt treatment of cases with appropriate antimalarial drugs. Further the proper deployment of antimalarials by implementing NMEP drug policy is must for avoiding the development of drug resistance. In the view of emerging problem of drug resistance the States have to build up their own capacity for conducting the drug sensitivity studies.

I. INTRODUCTION

NATIONAL MALARIA ERADICATION PROGRAMME

The National Malaria Control Programme (**NMCP**) was launched as early as 1953 and consequent to the encouraging results achieved, NMCP was switched over to National Malaria Eradication Programme (**N.M.E.P.**) in 1958. With the launching of NMEP there was a spectacular decline in malaria in the country which came down from approx. 75 million estimated cases in 1947 to 0.1 million cases and no deaths due to malaria in 1965. The success achieved by the National Malaria Eradication Programme was short lived due to various constraints of financial, logistic, administrative and technical nature and malaria started resurging and reached a peak of about 6.47 million malaria cases in 1976. With the resurgence of malaria especially during the seventies and reports of resistance Plasmodium falciparum to chloroquine in some pockets of the country posed a serious threat than ever before.

The resurgence warranted a revised strategy and so the Modified Plan of Operation (MPO) was launched in the year 1977 which made provision for intensification of various activities especially in areas where *P.falciparum* was found to be a dominant species, evidence of the existence of foci of chloroquine resistant *P.falciparum* malaria.

Since the implementation of MPO there has been a gradual reduction in malaria incidence which has stabilized to around 2 million cases annually. Till 1993, although the overall Malaria situation has remained the same during that period yet there was a trend of continuous rising of *P.falciparum* cases in proportion to the total malaria incidence. Deaths due to malaria were being reported regularly from year 1975 onwards. From 1994 there has been a sudden upsurge of malaria in the country due to many focal outbreaks reported from the various parts of the country. Reported deaths due to malaria in 1994, 1995 and 1996 are 1122, 1151 and 1010 respectively.

The Programme was reviewed by the Expert Committee in December 1994 which has recommended the intensification of malaria control activities throughout the country with focus on High Risk Areas through an **integrated Malaria Control Strategies** which has the following components:-

1. Early case detection and prompt treatment (EDPT)
2. Selective Vector Control
3. Promotion of personal protection methods
4. Early detection and containment of epidemics

5. Information, Education and Communication towards personal prevention and Community participation.

6. Institutional and Management capacity building, trained manpower development and efficient Management Information System (M.I.S.).

CHEMOTHERAPY OF MALARIA

Malaria diagnosis is carried out by microscopic examination of blood films collected by active and passive agencies. In general , presumptive treatment is given at the time of blood smear collection and radical treatment to confirmed malaria patients after the results of blood examination. The treatment schedule varies from area to area depending on endemicity and status of resistance to antimalarials. The chemotherapy is one of the most important aspect in the programme. The timely administration, of appropriate antimalarial is very important for management of malaria patient as well as for effective control of malaria. The national drug policy for NMEP has been evolved with the objective of proper deployment of antimalarial drugs and effective and judicious use of antimalarials for the treatment of malaria cases.

EMERGENCE OF CHLOROQUINE RESISTANCE

Chloroquine continues to be used for the treatment of malaria cases since the 2nd world war. However , inspite of extensive use of chloroquine, emergence of resistance to this drug in human malaria had not been reported prior to 1960. *P. falciparum* resistance to chloroquine, the most widely used drug, was almost simultaneously detected in Colombia and Thailand (1960). Later on, other countries of South East Asia like Bangladesh, Indonesia, Malaysia, Vietnam, Cambodia and Myanmar reported number of foci of chloroquine resistance.

In India, first confirmed report of chloroquine resistance in *P.falciparum* was reported in 1973 from Diphu of Karbi-Anglong district and then in 1974 another resistant focus was detected in Nowgaon district, both in the Assam state. Thereafter several tests were carried out in the states of Orissa, Tamilnadu, Karnataka, and Madhya Pradesh during 1973-77, but did not reveal any focus of resistant strain of *P.falciparum* in these states. A large number of tests carried out in the north-eastern parts of India indicated that chloroquine resistance in *P.falciparum* was quite wide spread in the states of Assam, Arunachal Pradesh, Mizoram and Nagaland. These observations necessitated the monitoring of drug sensitivity on a wider scale. With the launching of a modified plan of operation (MPO) emphasis was laid on chemotherapy of malaria.

A systematic study on monitoring of drug resistance throughout the country were initiated by the government of India from 1978. The main objectives of the study was

- To assess the sensitivity of *P.falciparum* to chloroquine by establishing a monitoring system to determine the spread, relative prevalence and degree

of resistance with a view to facilitating the implementation of operational counter measures.

- To assess the response of *P.falciparum* to antimalarials other than chloroquine

At present 13 *P.falciparum* monitoring teams including a team to conduct trials with various antimalarials are working under the direct supervision of Regional Directors, Regional Offices for Health and Family Welfare in various parts of the country. These teams conduct studies in areas falling in the territorial jurisdiction of the concerned regional office. The activities of these teams are coordinated by a central team located in the directorate of NMEP, Delhi.

The area of operation for each team is allocated in such a way that the entire country can be surveyed and mapped. Each team is headed by a Research Officer (medical) and 8 laboratory assistants and ancillary staff. Teams are provided with vehicle for mobility , equipment and other materials required for the study. The findings of these studies are communicated to the concerned state health authorities with guidelines to gear up surveillance and to take timely measures for the containment/liquidation and prevention of spread of resistant foci.

Although these teams have been able to provide information regarding the sensitivity status of P.falciparum to chloroquine but it is being realised that a substantial information on longitudinal monitoring is paramount importance to the programme in formulating a appropriate drug policy in the country. Therefore the states have been asked to constitute their own teams for wider coverage . It is expected that by the end of 1998 at least 5-6 states will develop their capacity for conducting drug sensitivity studies. The in-vivo tests with standard 7-day and an extended 28-day test as recommended by WHO are being followed , according to the need.

II. TEST METHODOLOGY

Drug resistance in malaria has been defined as the "ability of a parasite strain to survive and/ or to multiply despite the administration and absorption of a drug given in doses equal to or higher than those usually recommended but within the limits of tolerance of the subject" (WHO, 1965, 1973).

The first standardized test system for the assessment of in-vivo response in Plasmodium falciparum were developed by WHO in 1965, shortly after the first reports of chloroquine resistance in this species These test systems were subsequently revised in 1967. The WHO Scientific Group on the Chemotherapy of Malaria and Resistance to Antimalarials-1972 , accepted these test methods and recommended to be followed . The standardized tests were originally developed for chloroquine but, with the appropriate modifications, they lend themselves also to the evaluation of the response to other blood schizonticidal drugs.

These tests follow set criteria for the selection of patients, the administration of the standard treatment regimen of the appropriate drug and daily parasitological blood examination for the stipulated period e.g. 7 or 28 days as the case may be.

CRETERIA FOR AREA SELECTION

Selection of area for study is very important and is the first step in assessing the response of *P. falciparum* to any antimalarial drug.

1) Areas with intense malaria transmission with P.falciparum predominance

2) Area from where therapeutic failure to conventional antimalarial drugs has been reported by Medical Officers of Primary Health Centres.

3) In areas with malaria outbreaks and high mortality.

4) Project areas with congregation or sudden inflow of population from endemic areas.

5) Repeat studies where resistance has already been detected.

SAMPLE SIZE

Although it is difficult to define the exact number of cases to be screened but as per WHO recommendations a sample size of about 30-35 patients should be taken up for screening in a given area. For taking a decision to change the anti-malarial drug in any area, a study sample of minimum of 30 cases is required.

INCLUSION CRETERIA FOR STUDY CASES

- P.falciparum cases with minimum parasitaemia of 1000 asexual parasites per cubic ml. of blood are screened for study through mass fever surveys and also from fever cases attending OPDs of PHCs / dispensaries.

- Cases with negative history of prior chloroquine intake and confirmed by urine examination are selected for study.

- The ideal cases are patients having fresh infection of P.falciparum without much immunity.

- Serious cases of malaria with complications and mixed infection should not be selected for the test.

THE IN-VIVO TEST

The objective of this test is to determine the effect of a treatment on the parasitaemia (asexual forms) of a case of malarial infection.

* The test is applicable to all species of human malaria;

* The test is applicable to all antimalarial drugs that are active against the asexual blood stages (blood schozonticides).

A. **7-Day field test** in which chloroquine 25 mg/kg body weight is administered during a period of three days with a observation period of 7-days.

Day 0.....10 mg/kg bd.wt.

Day 1.....10 mg/kg bd.wt.

Day 2.....5 mg/kg bd.wt.

Before the administration of drug on Day 0, a thick and thin blood smear is collected . After staining with Gumsa asexual parasites are counted against 1000 WBC and recorded as initial parasitaemia. Blood smear examination is to be carried out daily from day 0 up to Day 7.

B. **28-Days extended field test**. The chloroquine dose remains same, i.e. 25 mg/kg bd.wt., spread over three days, but the observation period is of 28 days. In this test the additional examinations are carried out on day 14, 21 and 28.

The 7 days test provides rapid information on the presence of RII and RIII level of resistance. The 28 days extended test is more appropriate to indicate the difference between the sensitive strain or strains with a RI resistance pattern.

As in some instances, non response to treatment is due to erratic absorption / incomplete absorption or delay in absorption of drug not because of resistance . Therefore in all cases, chloroquine excretion test in urine by Dill and Glazko method is carried out once before administration of drug and subsequently on the second or third day after administration of the drug to ensure that the chloroquine was in fact absorbed in the blood.

EVALUATION :

Evaluation of test is done on the following clinical and parasitological status ;

- Time taken for clearance of symptoms (clinical improvement).
- Time taken for reduction in density / clearance of asexual stages of parasite.
- Observations will be followed for at least 4 weeks and blood slides will be examined periodically for recrudescence.

INTERPRETATION OF WHO STANDARD IN-VIVO FIELD TEST (7-DAY TEST)

- If no asexual parasites are found by day 6 and none are present on day-7, the infection may be either sensitive (S) or Resistance at RI level.
- If asexual parasites disappear for at least 2 consecutive days but return and are present on day-7, they are resistant at RI level.
- If asexual parasitaemia does not clear but is reduced to 25% or less of the original pre-test level during the first 48 hours of treatment, the parasites are resistant at RII level.
- If asexual parasitaemia is reduced by less than 75% during the first 48 hours or if it continues to rise, the parasites are resistant at RIII level.

Note: Resistance at the RIII level may exists when the count on Day-2 markedly exceeds the count on Day-0. In this case the test should be suspended and the patient should be given effective treatment if his clinical condition so demands.

Serious cases of malaria with complications and mixed infection should not be selected for the test.

INTERPRETATION OF AN EXTENDED TEST (28 - Day Test)

This test will distinguish between sensitivity (S) and the level of resistance and is interpreted as follows:

- If no asexual parasites are found on Day-6, and parasites do not reappear by Day-28, they are sensitive(s).

- If asexual parasites disappear as in above but return within 28 days and re-infection having been excluded, the parasites are resistant at the RI level.

- Interpretation of RII and RIII remains the same as for 7 Day test. (See note under 7 day test above).

THE IN-VITRO TEST

A standardised in-vitro (micro) test kit was developed by WHO in 1978 to determine sensitivity of *P.falciparum* to antimalarials viz. chloroquine, amodiaquine, quinine, mefloquine and sulfa pyremethamine combination. The test is based on the incubation of parasitaemia of capillary blood samples in a low para-aminobenzoic acid low folic acid RPMI-1640 medium in microtest plates pre-dosed with drug. The effect of the drug is assessed by measuring schizont development in a series of 8 geometrically increasing drug concentrations after 24-30 hours incubation at 37.5°C.

Experience in malaria control programme has shown that in-vitro test of parasite sensitivity to antimalarial drugs can not substitute for in-vivo observations on malaria therapy but they are a useful research tool to provide background information for the evaluation of drug response and for monitoring the pattern of cross-resistance.

III. STATUS OF DRUG RESISTANCE IN INDIA

Current status of chloroquine

The first confirmed report of P.falciparum focus resistance to chloroquine was detected in 1973 in the district of Karbi-Anglong and then in the subsequent year in Nowgaon, both in Assam. Though regular and systematic monitoring of drug resistance was initiated in 1978, only few states could be monitored in the initial years.

From 1978 till 1997 the monitoring teams conducted in-vivo studies on 12,863 Pf. cases. Summary of cases tested is given in Table-1. Analysis of year wise in-vivo cases tested (Table-2) shows increasing proportion of RII and RIII resistance to chloroquine with gradually increasing Pf. incidence in the country (Fig.1). The increase in RII and RIII findings can not be purely attributed to rise in RII and RIII proportion in old foci but increase is also on account of new areas reporting RII and RIII.

Till 1983 chloroquine resistance to P.falciparum at various levels was detected in the states namely Arunachal Pradesh, Andhra Pradesh, Bihar, Madhya Pradesh, Maharashtra, Meghalaya, Mizoram, Orissa, Tripura, Uttar Pradesh, Karnataka, West Bengal and Andaman Nicobar Islands . Subsequently chloroquine resistance in P.falciparum was detected in other states of Rajasthan, Gujarat and Tamilnadu. During 1997, resistance was detected among the migratory population in the state of Goa. The U.T. of Dadra and Nagar Haveli also reported high level of resistance during 1997 from indigenous population. In-vivo resistance status to chloroquine fulfilling the criteria of sample size of 30 or more is shown in Fig-2 which clearly indicates that a high degree of resistance is generally confined to the North-Eastern states barring the states of Tripura and Manipur and some other states in the Western belt. On the basis of the studies, alternative anti-malarial, i.e., sulfa-pyremethamine combination, has been introduced as shown in fig. 2 where 25% or more RII and RIII levels of resistance detected. However, higher degree of resistance has also been recorded in studies having a smaller low sample size as shown in fig. 3.

As seen from the fig. 2 and 3, the distribution of resistance levels indicates that resistance to chloroquine can be expected in any area with intense Pf transmission. In areas where the ecosystem sustains stable transmission of Pf malaria, the immunity in the population prevents rapid development of resistance to highest levels. In areas which allow intermixing of immune and semi-immune population and also provides conducive ecosystem for Pf transmission the development of resistance is rapid.

In hyper-endemic areas which predominantly Pf there is a discernible trend towards increase in frequency and degree of resistance to chloroquine. The northeastern sector in the Indo-Chinese peninsula experiences stable endemicity with predominantly Pf barring a few districts in the Brahmaputra valley. Apart from intense Pf transmission there is a constant population movement particularly across the international border with Bangladesh. Resistance is high and widespread in these areas. It has also been observed

that in Project areas which aggregate a large body of labour force there is a tendency of increased resistance as was detected in Visakhapatnam steel plant and other project areas and around construction projects in Bombay and Delhi. On closer scrutiny it is observed that high degree of resistance in the northern and southern parts of the country are confined to project areas which attract large labour force with differential immune status from various parts of the country. The risk of Pf malaria in these areas is restricted to the small population in the project area. Similarly the high resistance observed in some of the districts of western India are confined to rapidly developing industrial cities in the tribal belt with rapid charges in the demographic profile for instance the districts of Surat, Baroda and Ahmedabad.

The low and focal resistance along the eastern coast gradually merging with the agency tracts with low and widespread resistance is a reflection of Pf transmission being confined to this tribal belt with larger population at risk of Pf malaria than that immediately along the shores. The low level of resistance in these areas can be explained by the fact that apart from the acquired immunity in the population supplementing the therapeutic effect of the drug, movement and consequent intermixing of population is very limited.

Sensitivity Status of other antimalarials

Large number of studies have been conducted with alternative drugs like amodiaquine, sulfa pyremethamine and quinine etc.

Amodiaquine was in use since 1983 in certain districts with high degree of resistance to chloroquine for presumptive treatment of all fever cases. This drug was considered to be marginally superior to chloroquine, however studies carried out from 1989 to 1996 in chloroquine as well as amodiaquine use areas in the northeast to determine the comparative efficacy of chloroquine and amodiaquine in the treatment of Pf malaria indicate Amodiaquine has no advantage over chloroquine resistant areas. Both the drugs have shown a similar response and considering the toxicity associated with amodiaquine it has been withdrawn from the Programme as per the drug policy 1995.

In-vivo drug resistance studies with sulfa-pyremethamine and quinine were conducted on 1075 and 209 Pf cases respectively. Sulfa-pyrimethamine drug combination were introduced as a second line of treatment in chloroquine resistant areas as per the NMEP drug policy. Study results have shown resistance to this drug combination in low proportion in the north-eastern states, West Bengal and Kolar district of Karnataka only .

Summary of the cases tested against each drug are given in table-1 (fig4).

IN-VITRO TEST

In-vitro tests were conducted with chloroquine, amodiaquine sulfa-pyrimethamine combination , quinine and mefloquine. Areas showing resistance of each drug is in

Table-1 (Fig.5). Resistance to mefloquine was observed in the district of Surat in 23.6% of the isolates but in East Godavari only 1 isolate was studied which was found resistant . Resistance to mefloquine though can be expected in Surat district because of reports indicating its very limited use by private practitioners or could be due to cross resistance precipitated by Quinine which needs to be investigated.

Table 1

PRESENT STATUS OF MALARIA DRUG RESISTANCE (CUMMULATIVE UPTO 1997)

In-vivo						In-vitro		
No.of cases tested	**S**	**S/RI**	**RI**	**RII**	**RIII**	**No.of cases tested**	**S**	**R**
DRUG CHLOROQUINE								
12863	3814	5984	1932	653	480	627	331	296
DRUG AMODIAQUINE								
333	116	99	61	35	22	36	4	32
DRUG SULFA-COMBINATION								
a) Sulfadoxine/Pyrimethamine								
915	256	639	10	6	4	8	8	0
b) Sulfalene/Pyrimethamine								
160	135	23	2	0	0	-	-	-
DRUG MEFLOQUINE								
-	-	-	-	-	-	104	97	7
DRUG QUININE								
209	171	23	13	2	0	21	19	2

TABLE 2:

IN-VIVO CHLOROQUINE SENSITIVITY STUDIES (YEAR-WISE)

YEAR	TOTAL CASES TESTED	NO. SENSITIVE	NO. S/RI	NO. RI	NO. RII	NO. RIII	RII + RIII %	Pf %
1978	526	473	44	4	3	2	1.0	13.24
1979	704	572	64	43	15	10	3.6	18.22
1980	644	452	89	74	26	3	4.5	20.29
1981	392	252	45	76	17	2	4.8	21.83
1982	457	253	71	95	31	7	8.3	25.25
1983	289	146	87	46	9	1	3.5	29.77
1984	434	227	160	36	11	0	2.5	30.01
1985	484	89	311	61	22	1	4.8	29.23
1986	568	183	121	217	39	8	8.3	35.61
1987	763	300	85	319	31	28	7.7	37.19
1988	600	185	76	250	27	62	14.8	36.95
1989	498	92	250	87	20	49	13.8	36.87
1990	679	137	298	158	48	38	12.7	37.25
1991	541	102	311	50	34	44	14.5	43.38
1992	1045	134	646	135	61	69	12.5	41
1993	864	64	603	63	67	67	15.5	38.5
1994	793	6	663	34	62	28	11.3	39.4
1995	1096	59	872	59	74	32	9.7	39.7
1996	888	73	689	82	26	18	5.0	37.5
1997	598	15	499	43	20	21	6.8	35.4-

Figure No. 1

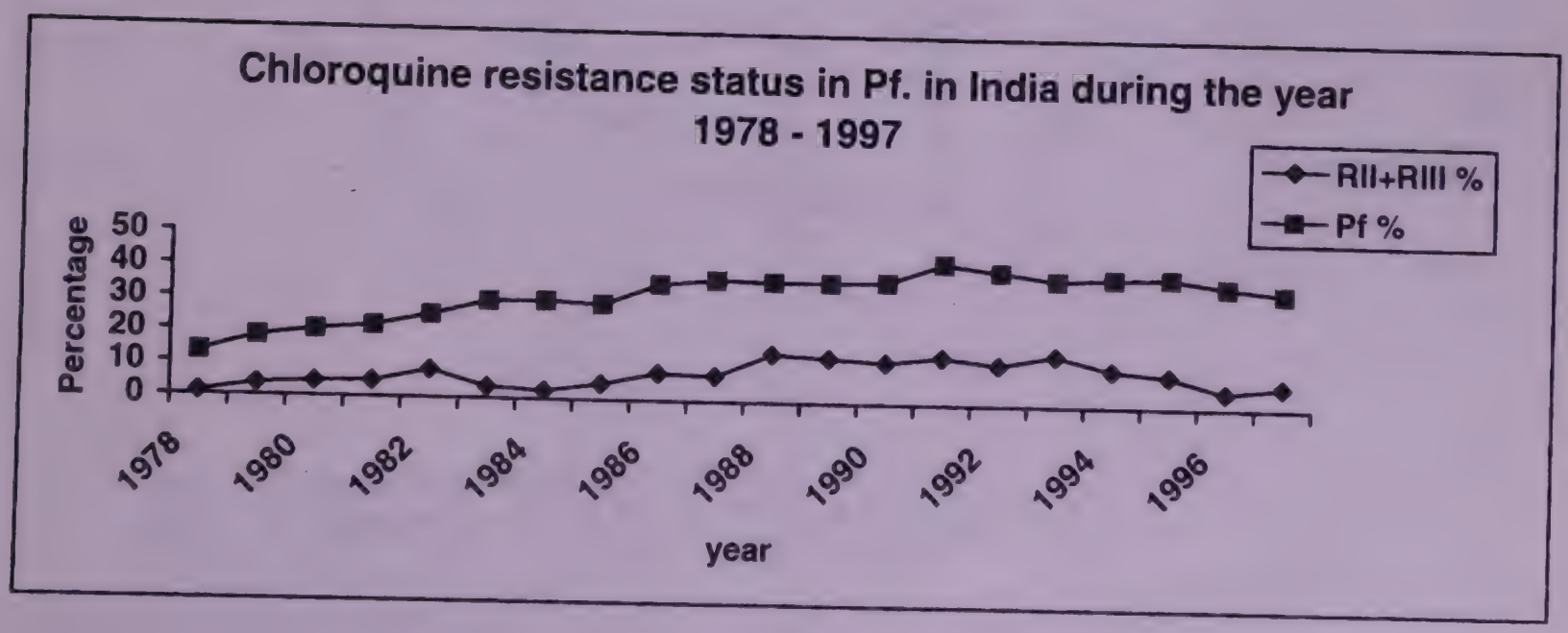


FIG- 2 DISTRIBUTION OF RESISTANCE IN SAMPLE SIZE 30 OR MORE

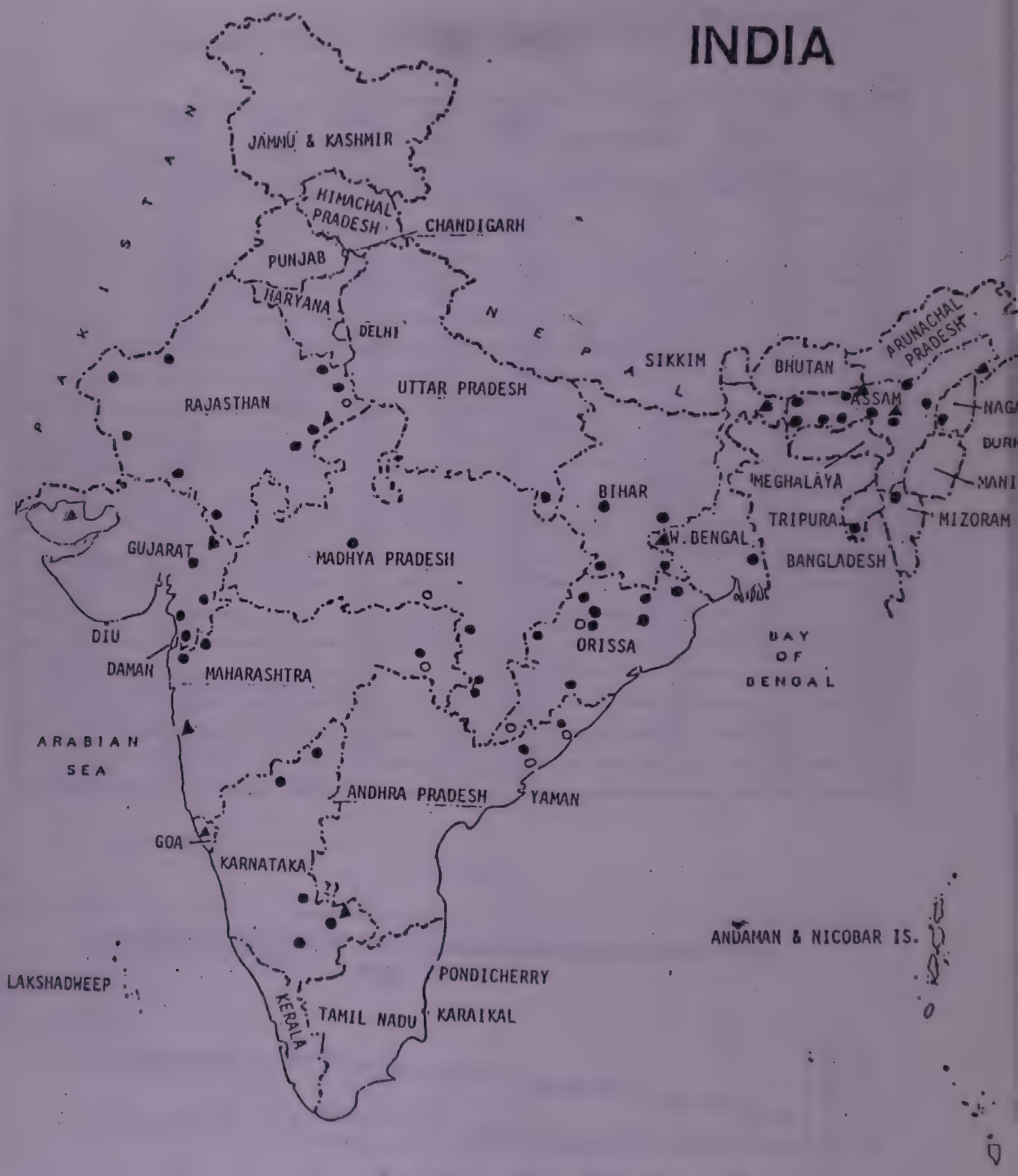
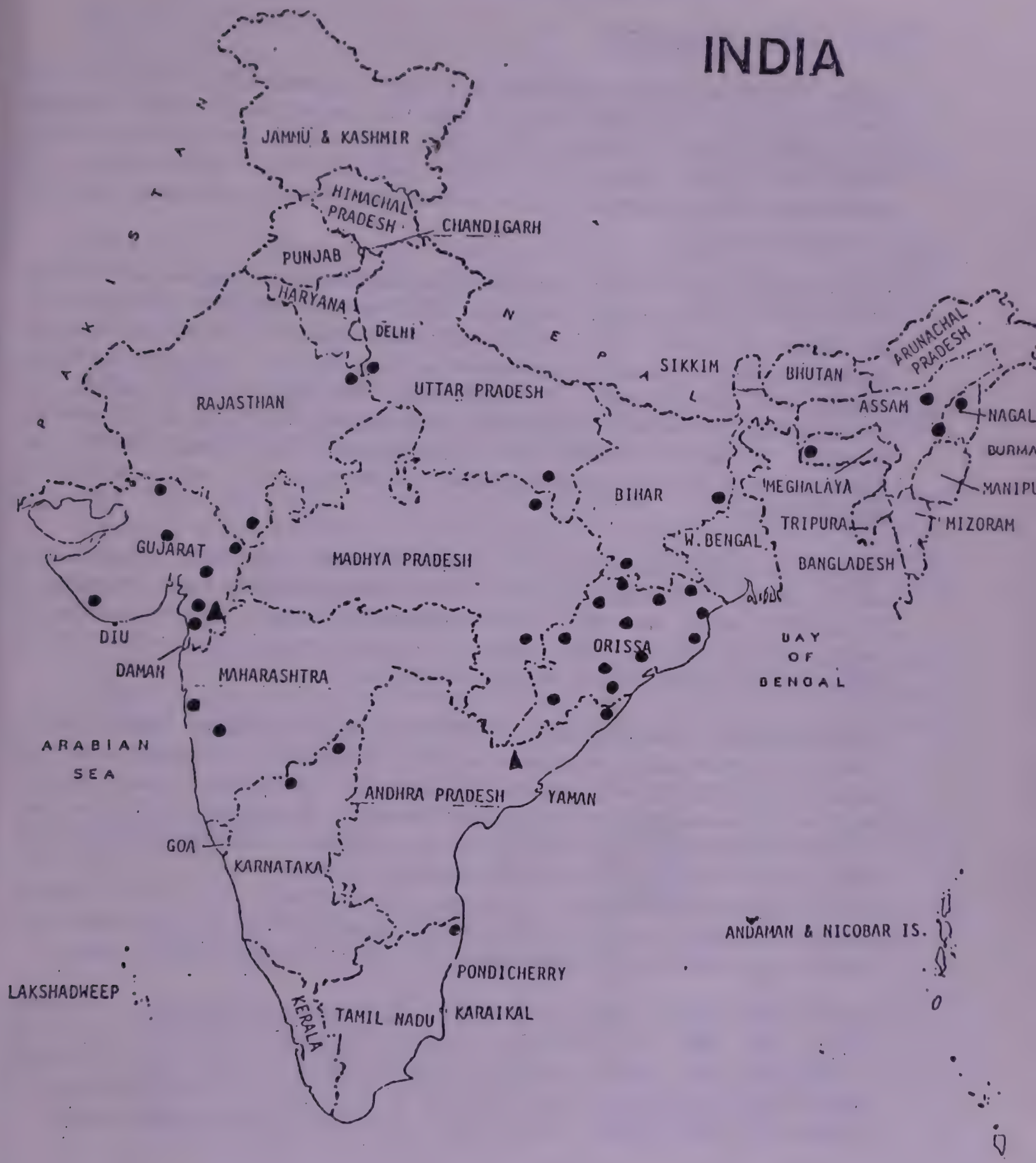


FIG- 3 DISTRIBUTION OF RESISTANCE IN SAMPLE SIZE < 30 CASES

FIG- 4 IN-VIVO RESISTANCE TO SULPHA PYREMETHAMINE COMBINATION

● RI or RII Resistance to Sulpha/Pyremethamine
▲ RIII Resistance to Sulpha/Pyremethamine

FIG-5 IN-VITRO SENSITIVITY STATUS TO DIFFERENT ANTIMALARIALS



● Resistant to chloroquine and amodiaquine
▲ Resistant to Mefloquine

VII. STATE-WISE STATUS OF DRUG RESISTANCE

VII.1. ANDHRA PRADESH

Andhra Pradesh with an area of 275068 sq.km. has a population of 64.5 million. The state is divided into 23 revenue districts with 1283 primary health centres. The state has varied ecological conditions from coastal, plain to hilly forested regions with drought prone areas mainly in the western parts. The hilly forested areas with predominantly tribal population is in the northern part of the state extending from east to west (Agency tract).

Malaria incidence as well as Pf. incidence in the state has shown marginal increase from 1993 to 1996. Malaria incidence has been 125414 cases during 1996 with 46.33 % Pf and API of 1.95 (SPR 1.47, SfR 0.9). Incidence of malaria is not uniform in all the districts. The districts located in the northern part (Agency tract) are stable and hyper-endemic with high proportion of P.falciparum. The districts with high Pf. are Visakhapatnam, E.Godavari, Srikakulam, Karimnagar, West Godavari, Khammam, Warangal, Prakasham, Adilabad and Vijaynagaram. The principal vectors are *An.culicifacies* in rural areas with *An.fluviatilis* in the agency tract and *An.stephensi* in the urban areas.

Migration to and from these districts are limited to neighboring districts within the state and the districts of Koraput (Orissa), Bastar (Madhya Pradesh) and Chandrapur (Maharashtra), which have similar eco-epidemiological features. These migrations are mainly for socio-economic reason. Seasonal migration for agriculture such as bamboo cutting and exploitation of forest produce is common.

The P.falciparum monitoring team of NMEP has been conducting studies for the detection of chloroquine resistance since 1979. Resistance to chloroquine has been detected in the districts of E.Godavari, Visakhapatnam, Khammam, Kurnool, Srikakulam, and Vijaynagaram. In the districts Warangal, Prakasham, W.Godavari and Adilabad no resistance was detected. As of date resistance to chloroquine is at RI level though few stray cases of RII and RIII resistance have been detected. In the state as a whole the status of resistance to chloroquine has not changed in the last two decade. Excluding the higher resistance detected in the Visakhapatnam steel plant area in the last five years there is no significant difference in the resistance status in the state.

EAST GODAVARI : Population of district is 3.71 million. In the district as a whole API was 2.45 (SPR - 1.5; SFr- 0.3). It has 55 PHCs out of which 6 of them in the forested hilly areas have predominantly Pf transmission. Chloroquine sensitivity studies have been conducted in 6 PHCs and all the areas have reported RI level of resistance. RII and RIII have been detected in Rajavomangi and Mredumilli PHCs.

In-vitro resistance to mefloquine was detected in 1988 in the single isolate studied . Since mefloquine has not yet been introduced in the programme and this area is least likely to have access to the drug further investigations are necessary.

VISHAKAPATNAM : Population is 3.50 million . Malaria transmission in the district has been high with API 8.62 (SPR-4.2, SFR-2.0). Resistance to chloroquine is at RI level in the district though RII and RIII levels were detected only from the steel plant area which no longer holds good as the total number of Pf cases in this area declined to 35 (1994) from 3371 (1989) consequent to the departure of the labour population after completion of the project. Resistance to chloroquine is therefore considered low and focal.

KHAMMAM : Population is 2.0 million having hilly forested areas where malaria incidence is high with predominantly P.falciparum with API 3.4 (SPR-1.85, SFR-1.69). Resistance to chloroquine is at RI level though one case of RIII was recorded during 1990 in one PHC. Resistance to chloroquine is low and focal.

SRIKAKULUM : Population is 2.25 million. The hilly and forested areas reporting high incidence of falciparum malaria. Malaria transmission is high with API 4.06 (SPR 2.5, SFR-2.2). Only in-vitro study revealed resistance in the year 1984.

KURNOOL: Population is 2.50 million and the entire district is plain area with mining and irrigation projects. Malaria is endemic in the district with API 3.89 (SPR-2.5, SFR-0.84). Only one PHC i.e Palukar PHC has high incidence of malaria but low proportion of Pf. Only one out of 7 cases studied during 1985 was at RI level. Resistance to chloroquine is considered low and focal.

VIJAYNAGARAM: Population is 1.9 million with moderate incidence of falciparum malaria. Malaria transmission is low with API 2.13 (SPR-1.14, SfR-0.98). Chloroquine resistance conducted during 1995 showed only RI level of resistance and is considered low and focal.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	E.Godavari	Rajavomangi	1981	45	23	1	0
		Maredumilli	1993	96	4	4	4
		Y.Ramavaram	1994	39	0	1	0
2	Visakhapatnam	Donuru	1982	52	0	0	0
		R.J.Palem	1996	34	1	0	0
		Steel Project	1988	43	17	5	5
		Area	1991	30	0	2	1

VII.2. ARUNACHAL PRADESH

Arunachal Pradesh is a state with an area of 83743 sq.km. and supports a population of 0.91 million. The state has 12 revenue district with 47 PHCs. The state is entirely hilly and forested.

Malaria incidence is high in all districts but P.falciparum is predominant in three districts namely Tirap, Changlang and Lohit which border Myanmar. The state maintains stable endemicity. During 1996 API was 53.84 (SPR-15.21, SFR-1.77). The principal vectors in the state are *An.minimus, An.dirus* and *An.fluviatilis*.

Migration to and from this state is limited in nature though some inter-country movement is present in the bordering areas. There is regular movement of armed forces to and other parts of the country.

The teams of NMEP have been conducting drug resistance studies since 1982 in the state with chloroquine, quinine, sulfa-pyrimethamine combination. These studies have been confined to two districts of Tirap and Changlang. In both the districts it was observed that in-vivo resistance to chloroquine is gradually increasing.

TIRAP: With a population of 0.09 million, the hilly forested district borders Myanmar. Malaria transmission is high with an API of 26.8 (SPR-14.9, SFR-2.9). Entire population is at risk of Pf malaria. In vivo resistance studies conducted since 1982 detected high proportion of RII and RIII. Drug policy has been changed in Jairampur PHC showing 30% cases at RII & RIII level. Resistance to chloroquine is considered high and widespread.

CHANGLANG: With a population of 0.094 million the district is hilly and forested bordering Myanmar. Malaria transmission is intense with an API of 84.5 (SPR-18.5, SFR-5.1). Entire population is at risk of Pf malaria. Resistance studies conducted since 1988 detected a fair proportion of RII and RIII cases. Chloroquine resistance is considered high and widespread.

In-vivo resistance at RII and RIII level to sulfadoxine-pyrimethamine (3 tabs stat) was detected in 1992 in 5.3 percent of tested cases.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Tirap	Jairampur	1982	30	18	6	3
2	Changlang	Miao	1992	56	18	8	4

VII.3. ANDAMAN AND NICOBAR ISLANDS

Andaman & Nicobar Islands have an area of 8249 sq.kms. with a population of 0.4 million. It comprises of a group of islands in the Bay of Bengal and the populace is served by 17 PHCs. Malaria incidence in the islands is around 1165 cases annually (SPR-0.56, SFR-0.10) with 18.7% of Pf cases. Incidence is relatively more in Nicobar group of islands (API-11.8, SPR-0.98, SFR-0.22) in comparison to the Andaman group (API-1.44, SPR-0.40, SFR-0.05). The principal vector in the island is *An.sundaicus*. Migration is very limited and does not involve the indigenous population.

Only four studies have been conducted in these islands since 1980. In Little Andaman 16% of the study cases were RI & RII in 1980 but in great Nicobar two resistant cases i.e. RI and RII were detected out of 19 cases studied. In Port Blair and Car Nicobar no resistance was detected in the studies conducted during 1980 and 1989 respectively. Resistance to chloroquine in Little Andaman & Great Nicobar is low and widespread.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	L.Andaman	Hut Bay	1980	49	3	5	0

VII.4. ASSAM

Assam has an area of 78438 sq.kms. supporting a population of 22.08 million. The state is divided into 23 districts with 619 PHCs. It is a state of hills and plains. The plain comprises mainly of the Brahmaputra valley about 720 kms. long and 80 kms. wide. Except for three districts in the valley the entire state has more than 33% of the land forested. The state borders Bangladesh in the South and Bhutan in the north. Assam state is the major contributor of malaria incidence in the North Eastern states. Malaria incidence in the state is around 176622 cases annually with 61% Pf cases (SPR-8.8, SFR-5.3) as per the 1996 data. Out of 23 districts 20 of them have high incidence of malaria with predominantly Pf. Malaria transmission is by and large stable with outbreaks restrict to area associated with temporary settlers. The principal vector in the state is *An. minimus* which is supported by *An.dirus* and *An.fluviatilis*. Transmission is perennial.

Large scale migration is associated with various projects such as in Tea estates, Border road organization and deployment of Armed forces. In addition to this inter-country movement particularly across Bangladesh border is a constant feature.

The Pf monitoring teams conducted resistance studies in 14 districts of the states since 1978. Resistance to Chloroquine was observed to be on the higher side. All the studies consistently detected high corporation of RI cases. Though RII and RIII cases were

detected in all the districts except two districts. Proportion of high level (RII and RIII) resistance varied from 3.2 to 77.7%. Resistance to the drug is increasing as there is gradual shift to the right in most districts. As per the revised drug policy (1981) second line of treatment with sulfa-pyrimethamine is being followed in two districts i.e Nawgaon & Karbi-Anglong. Amodiaquine was introduced in both districts Nawgaon and Karbi- Anglong in 1983 in lieu of Chloroquine for presumptive treatment. Studies with chloroquine and amodiaquine in the state detected no variance in the susceptibility of Pf both in chloroquine and amodiaquine used areas. Resistance to sulfa-pyrimethamine combination at RIII level and to quinine at RI level has been reported.

KARBI-ANGLONG : Population is 0.70 million with high incidence of Pf malaria (SPR-12.3, SFR-8.1). It has 11 PHCs and all are equally endemic for malaria. The ecology of the district is hilly and forested. This district was the first to report chloroquine resistance in India in 1973. In-vivo and in-vitro studies consistently detected resistance at all levels which is on the rise. Resistance to chloroquine is high and widespread. Because of high resistance the revised drug policy for Pf cases is being followed since 1983.

In-vivo resistance to sulfa-pyrimethamine at RI level was detected in 1979 but a study in 1991 detected 12% of cases resistant at RII and RIII level.

KAMRUP: Population is 2.0 million with 0.48 million residing in areas of high Pf. incidence. Malaria incidence is on the rise with API of 12.2.(SPR-10.0, SFR-8.4) and 6 out of the 16 PHCs are mainly affected. Ecology of the area is generally plain and foot hills. Studies since 1980 detected RII level of resistance but subsequent studies during 1987, 1990 and 1992 detected all level of resistance. Resistance to chloroquine is high and focal. Comparative studies with amodiaquine and chloroquine indicated no significant difference in the sensitivity status.

GOALPARA: Population is 0.81 million with the entire population at high risk of Pf malaria. API being 6.24 (SPR-5.24, SFR-4.11). The district consists of plain and foot-hill (forested) areas. Resistance to chloroquine was detected in 1982 at RI and RIII level. Subsequent studies also revealed resistant at RIII in low proportion . Resistance to chloroquine is considered low and wide spread. Comparative in-vivo studies with amodaioquine and chloroquine indicated no significant difference in the sensitivity status of the parasite.

SIBSAGAR: Population is 1.10 million and malaria incidence in the district is low API 0.02 (SPR-0.03, SFR-0.02). Terrain is mainly plain and foothills with scattered Tea estates. Drug resistance study was conducted in one tea estates which revealed resistance at all levels. Since the entire district experiences low malaria transmission, the population of the Tea estate which comprise of labour from different parts of the state are mainly at risk of resistant malaria. Resistance to chloroquine is low and focal.

NOWGAON: Situated on the plains and foothills with a population of 0.91 million has 0.63 million people residing in areas of high Pf incidence. Malaria incidence in the

district as a whole is on rise with API 37.54 (SPR-23.4, SFR-11.40). RII and RIII levels of resistance has been consistently detected in the district since 1985 but the proportion of resistant cases in the study sample has come down from 30% in 1989 to 6.5% in 1992. Resistance to chloroquine is high and widespread. Comparative in-vivo studies indicate that there is no significant difference in the response of the parasite to amodiaquine and chloroquine.

In-vivo resistance to SP combination was detected only in 1992 at RI level in 3.6% of cases.

KOKRAJHAR: The entire population of 0.73 million is at risk of malaria. Malaria incidence in the district is high and stable with API of 15.11 (SPR-8.2 SFR-6.5). All the 7 PHCs in the district are highly endemic for Pf malaria . The terrain is entirely hilly and forested. Only 3 in-vivo studies have been conducted since 1985. Though initially RII was detected subsequent study in 1988 revealed 17.6% resistant at RIII level . Resistance to chloroquine is low and widespread.

NALBARI: Population is 1.11 million out of which 0.33 million are residing in areas of high incidence of malaria. Malaria incidence in the district as a whole is high with API of 4.7 (SPR-6.3, SFR-5.6). Out of the 7 PHCs in the district only 2 are highly malarious. The terrain is plain and foot hills. In 1986 only RI was detected but further studies in 1990 and 1992 detected RII and RIII resistance also. Resistance to chloroquine is high and widespread. Comparative in-vivo studies with amodiaquine and chloroquine indicated no significant difference in the response rate. In-vivo resistance to SP combination at RII level was detected in 1992 in 10% of the low sample size.

DARRANG : Population is 1.42 million. Malaria incidence in the district is high with API-18.6 (SPR-14.5, SFR-1.01). Out of 7 PHCs, only 2 recorded very high incidence with predominantly P.vivax, Terrain is mainly foot hills with plain areas interspersed. Studies have been conducted since 1987 but RIII level of resistance was detected in the year 1993 and also in subsequent studies during 1994 and 1995. Resistance is high and widespread.

DHUBRI: Population is 1.45 million with 0.52 million living in highly malarious areas. Incidence in the district as a whole is high with an API of 4.8 (SPR-33.92, SFR-30.7). Terrain is generally plain in nature. studies conducted in 1990 and 1993 shows that 14.8% and 23.6 % are RII and RIII respectively. Resistance to chloroquine is widespread and high. Comparative in-vivo studies with amodiaquine and chloroquine indicated no significant difference in the response rate.

CACHAR: Population of the district is 1.4 million. API of the district has been 4.4, SPR-4.54 and SFR-4.52. Topography is mainly hilly and forested. A single study so far revealed one case each resistant at RII and RIII level from a total test sample of 3 cases. As the sample size was too small resistance to chloroquine is considered to be low and focal.

SONITPUR: Population is 1.65 million with 0.3 million living in highly endemic areas. API of the district is 9.9 (SPR-7.7, SFR-2.9). District is mainly hilly and forested. Out of 7 PHCs only 1 is reporting relatively high incidence. five studies were conducted and RIII level was detected in Balipara PHC only. Resistance to chloroquine is low and focal.

MORIGAON: This new district was created in 1991. The population of the district has been 0.63 with API 2.14 (SPR-1.74 and SFR-0.41). All levels of resistance to chloroquine were detected in a study during 1995. The RII and RIII level of resistance was 15% among sample of 40 cases. Resistance to chloroquine is presently high and focal.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Goalpara	Agia	1989	33	13	0	0
2	Karbi-Anglong	Manja	1979	131	24	5	6
		Manja	1984	41	7	0	0
		Manja	1986	58	7	1	0
		Bokajan	1986	46	17	3	0
3	Darrang	Hatigarh	1993	39	12	0	1
		Orang	1995	32	0	4	5
4	Kamrup	Sonapur	1980	41	11	1	0
		Boko	1983	52	18	1	0
			1985	32	1	1	0
			1987	47	32	4	1
			1992	33	13	2	3
5	Morigaon	Nelli	1995	40	1	3	3
6	Sonitpur	Ballipara	1989	32	22	2	2
		Biswanath	1996	32	0	0	0
		Chariali					
7	Nowgaon	Salona TE	1985	37	1	1	0
			1988	54	25	3	12
		Jakhalbanda	1992	31	1	1	1
		Simonbasti	1990	31	14	0	1
8	Kokrajhar	Sidli	1985	40	9	7	0
		Kochugaon	1986	30	11	2	1
9	Dhubri	Chappar	1993	34	1	7	1

VII.5. ***BIHAR***

Bihar has an area of 173877 sq.kms. and supports a population of 99.2 million. The state is divided into 39 revenue districts with 2209 PHCs. The entire state has two distinct ecotypes. North Bihar is plain and flood prone whereas southern Bihar is on a plateau which is hilly and forested.

South Bihar is endemic for malaria with high proportion of Pf cases. In the year 1996, 64859 cases of malaria were reported with 62% of Pf. The API in the state was low 1.06 but transmission is high as reflected by SPR 7.42 and SfR 4.6. Most of the cases are reported from South Bihar. All the 12 districts in south Bihar are highly endemic. The principal vector in the state is *An.culicifacies* and An.fluviatilis.

Migration within and out of the state is due to economic needs and though the same has not been quantified, movement is for agricultural purpose and other developmental projects.

Resistance to chloroquine in P.falciparum is being monitored in the state since 1980. Majority of the districts in South Bihar has been mapped for drug resistance. Resistance to chloroquine has been detected in the districts of W.Singhbhum, Dumka, Gumla, Godda, Ranchi, Hazaribagh, Patna, Pakur and Bokaro. RIII level which was detected for the first time in 1989 is confined to the five districts i.e Gumla, Ranchi and Hazaribagh, West Singhbhum and Bokaro. Overall picture indicates a gradual rise in the resistance level.

WEST SINGHBHUM: The entire population of 3.5 million live in the forested plains and foot hill areas which are highly endemic for Pf malaria. (SPR-13.7, SFR-13.6). All the 32 PHCs are equally endemic. Resistance studies conducted since 1980 reported RI & RII resistance in two PHCs. During 1996 RII & RIII level of resistance have been detected in new PHC but in low proportion. Considering the present situation of low proportion of RII and RIII cases the resistant level in the area is low but widespread.

DUMKA: The entire population of 0.6 million reside in low endemic area (SPR-0.02, SFR-0.82) with predominantly P.vivax transmission. Terrain consists of plain areas. A study in 1984 indicated resistance at RII level. In-vitro study in 1985 also indicated resistance. Resistance to chloroquine is low and focal.

GUMLA: The entire district is highly endemic with Pf and the total population of 1.23 million is at risk of malaria (SPR-15.3, SFR-13.0). The terrain is mainly plain and hilly with small areas of forest. Resistance in in-vitro and at RI level was detected in 1984 but subsequent studies during 1989 and 1992 RII and RIII level was reported. The level of resistance to chloroquine is considered high and widespread.

GODDA: The entire district with a population of 0.92 million experiences low malaria transmission (SPR-3.3, SFR-1.7) and the terrain is mainly plain. Out of four

studies conducted so far only in 1993 resistant at RII level was reported and therefore resistance to chloroquine is considered low and focal.

RANCHI: The entire population of 2.4 million is at risk of Pf malaria. Endemicity is high with SPR-6.4 and SFR-5.3. Terrain is generally plain with patches of forest. Resistance to chloroquine at RII and RIII level was reported in one of the PHC in 1990 but low proportion. Status of chloroquine is low and focal.

HAZARIBAGH: The total population of 2.26 million is at risk of malaria. Transmission is moderately high with Pf (SPR-8.0, SFR-1.3). The terrain is mainly undulating plains. Resistance was detected in 1992 in a sample of 23 cases wherein only 12.9% were found resistant. Subsequent studies detected 22.4% chloroquine resistance and therefore resistance level is considered on rise and wide spread.

PAKUR: The population of this newly created district has been 0.17 million. The terrain is mainly undulating plains. Resistance at RII level was detected in 1996 in a low sample of 4 cases only. Resistance is considered low and focal.

PATNA: It is in the northern plains of the state having a population of 4.0 million and experiences low level of malaria transmission (SPR-0.12, SFR-0.01). Resistance at RI level was detected in 1988 in 2 out of 7 cases tested. Since transmission potential is low, resistance to chloroquine is considered low and focal in nature.

BOKARO: The newly created district with a population of 0.33 million. This steel city draws large number of labourers from various parts of the state and also out side of state. The topography is hilly. Resistance studies conducted in the same PHC in 1994 and 1996 detected 9.5 and 5.4 per cent of RII and RIII level of resistance. Resistance is considered low and focal.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	W.Singhbhum	Novmundi	1980	46	5	3	0
		Novmundi	1994	30	1	1	0
		Manoharpur	1985	60	5	4	0
2	Gumla	Simdega	1992	37	3	1	4
		Palkot	1997	33	1	1	0
3	Hazaribagh	Bishnugarh	1995	33	1	1	3
4	Bokaro	Paterbar	1996	37	1	1	1

VII.6. DADRA AND NAGAR HAVELI

The Union Territory of Dadra and Nagar Haveli is having a population of 0.14 million served by 6 PHCs. The population of this union territory is basically tribal. The topography consists mainly of hills with forests. Rapid industrialization draws large number of labour population for construction work from highly malarious areas of the country. As conglomeration of labourers settle in shabby huts it further extend the influence of vectors *An.culicifacies* and *An.fluviatalis* and also the intensify of infection. The API in the year 1996 has been 82.9 (SPR-24.4, SFR-4.9). The incidence of Pf is on rise.

Chloroquine sensitivity conducted in 1997 among indigenous tribal population showed RII and RIII level of resistance in P.falciparum around 7.7 per cent. Resistance is therefore considered low and focal.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Dadra & Nagar Haveli	Dudhni	1997	91	1	5	2

VII.7. DELHI

Delhi situated on the banks of river Yamuna has a total area of 1483 sq.kms. with a population of 10.7 million. The state of Delhi is largely urbanised with 90% urban population. The rural populace is served by 8 PHCs. The topography consists of plain areas. It is a rapidly expanding city with major construction activities.

Malaria incidence in the state is low and is mainly P.vivax (SPR-0.77, SFR-0.05). There are pockets of high incidence of malaria which are confined to the housing and other civil construction works. As these areas aggregate labour from different parts of the country in temporary settlements they create mosquitogenic conditions conducive for increased malaria transmission. The prevalent vector species in the urban area is *An.stephensi* and *An.culicifacies* in the rural areas.

Resistance study was first conducted in 1984 and no resistance was detected but another study in 1992 around a housing project site where 3 cases were tested revealed resistance at RI and RII level. Resistance status in Delhi is therefore considered focal and at low level.

VII.8. GOA

The erstwhile union territory having 1.21 million population served by 21 PHCs. the topography varies from plain to hilly areas with rapidly expanding tourism centres. The construction activities draw large number of labour force from various parts of the country involving highly malarious areas like southern Bihar, Orissa, northern parts of Andhra Pradesh, Karnataka and also from Maharashtra.

Malaria incidence in the state is high and on rise. Particularly P.falciparum incidence with API-10.0 (SPR-7.71, SFR-1.02).

Resistance studies conducted in one PHC in 1997 among labour population showed 26.5 per cent RII and RIII level of resistance in P.falciparum to chloroquine. Presently resistance level is considered high and focal. Keeping in view the high level of resistance in the particular group of population, further studies are required to know the status of chloroquine sensitivity among the indigenous population.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	North Goa	Aldona	1997	34	1	3	6

VII.9. GUJARAT

Gujarat has an area of 196024 sq. kms with total population of 45.2 million. There are 19 districts with 957 PHCs. A Coastal state in the west having plains and hills in the eastern border partly covered by large forests. The tribal belt covers the districts of Banaskantha. Sabarkantha, Panchmahal, Baroda, Bharuch, Valsad, parts of Surat and Dang all situated along the eastern border.

Malaria incidence in the state is around 143817 cases during 1996 with 22.31% being Pf cases (SPR-2.0 , SFR 0.5). The districts bordering the states of Rajasthan, Madhya Pradesh and Maharashtra have high intensity of malaria transmission. The tribal districts experience high Pf transmission. The principal vector is *An.culicifacies* in the rural areas but in the foothills particularly in the tribal belt it is *An. fluviatilis.*

The resistance studies conducted since 1978 for chloroquine have demonstrated high degree of resistance in the districts of Kutch-Bhuj, Surat, Valsad and Banaskantha. Till 1984 no resistance was detected but subsequent studies especially in the districts of Surat, Valsad, Banaskantha, Kheda, Ahmedabad Baroda city and Kutch-Bhuj indicated a shift to the right with higher proportion of RII and RIII cases. Studies conducted in

the district of Surendranagar and Bhavnagar showed no resistance to chloroquine. In this state as a whole the resistance to chloroquine has been gradually increasing. Stray cases of in-vitro resistance to mefloquine has been detected.

SURAT: The population of the district is 3.9 million and 50 % of the population is residing in Surat City. The entire district can be divided into three ecosystems with an eastern tract of hilly land and fertile plains in the middle merging with the coastal industrial belt in the west. The entire district is hyperendemic for malaria aggravated by rapid industrialisation and urbanisation of Surat City. The magnitude of transmission is API 10.60 (SPR-5.3, SFR-2.0). In-vivo and in vitro studies conducted prior to 1984 detected no resistance to chloroquine. RI resistance(14%) was first detected in Urban PHC (1984) and later RII and RIII levels of resistance in gradually increasing proportion was detected in other PHCs. Resistance to chloroquine is high and widespread. In-vitro resistance to amodiaquine and mefloquine was detected in 1987.

BANASKANTHA : Has a population of 2.43 million. Most of the areas of the district are plain. Malaria endemicity is low having API of 0.6 (SPR 0.37, SFR 0.02). Resistance studies carried out in Wav and Tadav PHC detected RI and RII resistance in low proportion. Resistance to chloroquine is therefore low and focal.

PANCHAMAHAL : Panchamahal district has a population of 3.23 million. The terrain of the district is largely irrigated plains close to the foothills of Aravali range. Malaria endemicity is low with API 0.57 (SPR 3.2 : SFR 0.34). Resistance studies (5) carried out since 1980 detected RII and RIII cases. In 1993 in Kadana PHC 11 cases out of 32 were resistance. Drug policy has been changed in Kadana PHC to second line of treatment i.e Sulfa-pyrimethamine combination following detection of high level of resistance in 1993. During repeat studies in 1994 no suitable cases were found. Resistance to chloroquine is high and widespread.

BHARUCH : Population of the district is 1.68 million. An endemic district with API 5.11 (SPR-3.04 : SFR-0.7). Topography ranges from foothills in the east and coastal plains in the west. Resistance studies were carried out in Lacharas PHC in 1987 and in 1990. In the first study of the 25 cases studied 16% were at RII level but in later study only 1 out of 13 cases being resistant at RII level. Studies conducted in other PHC in 1997 showed RII level resistance. Resistance status of chloroquine is considered low though widespread.

JUNAGADH : Junagadh is a coastal district having a population of 2.6 million. The population residing in 15 PHCs i.e. 35% of the total is under high malaria transmission. Malaria transmission is moderate with API 2.7 (SPR-2.3, SFR-0.44). Resistance at RI level was detected in 1986. In 1993 one case out of six reported RIII level of resistance. Resistance status to chloroquine is low and widespread.

VALSAD : The population of the district is 2.39 million. The ecology of the district is generally hilly and forested though irrigated plain areas are present. Malaria transmission is high with API 5.13 (SPR-3.02: SFR-1.03). The resistance studies

carried out since 1986 have shown varying degrees of resistance. Though RII and RIII resistance have been detected but in low proportion . In 1995 6.7% out of 89 cases have been detected at RII level of resistance. Resistance to chloroquine is low and widespread.

BARODA: Baroda district has a population of 3.4 million and is endemic for malaria with API 3.4 (SPR-2.1, SFR-0.43). Resistance studies carried out since 1982 detected resistance in Baroda city and Atahadungri PHC. Though RII and RIII cases have been detected the combined proportion never exceeded 15% of the test sample in Baroda City. Resistance to chloroquine at the RII and RIII level in another PHC of the district has been observed in 1997 upto 4.1% resistance . The resistance is therefore is low but widespread.

AHMEDABAD : Ahmedabad district has a population of 1.93 million. Malaria transmission on the whole is low with API 1.3 (SPR-0.6, SFR-0.08). Ahmedabad is mainly an industrial town with population coming from within and outside the state. The resistance study carried out in 1989 detected 7 cases out of 24 resistant with 20.8% at RII and RIII level. In-vitro study also indicated resistance and though resistance to chloroquine is relatively low it is focal in distribution.

AMRELI : Population of the district is 1.3 million and the terrain is mostly plain adjoining the sea. Malaria incidence is moderate with API 2.8 (SPR 1.63 : SFR-0.2). Only 18% of the population in 7 PHCs is under high malaria transmission. Studies revealed low level of resistance to chloroquine which is focal in distribution.

DANGS : Population of the district is 0.16 million and the terrain is mostly undulating plains. The district is hyperendemic with API 11.83 (SPR 5.4 SFR 0.86) but Pf transmission is intense in 2 PHCs which support 45% of the total population. Resistance studies carried out in Sudhir PHC revealed low level of resistance as only 6.7% of the test cases were resistant. Therefore resistance status of chloroquine is low and focal.

KHEDA : The population of the district is 3.67 million and most of the district is plain irrigated land. Malaria transmission is moderate with API 3.12 (SPR-1.7, SFR-0.7). Studies carried out in 3 PHCs since 1991 have revealed resistance at all level. Though RII and RIII cases were detected the combined proportion was 20.6%. Resistance to chloroquine is low and focal in nature.

SABARKANTHA : With a population of 1.9 million the district is low endemic for malaria with API 1.74 (SPR-0.72 SFR-0.08). It has varied ecology of plains and undulating forested hills. RII and RIII cases were detected in high proportion of 57.7% in 1992 out of 26 cases studied. During 1993 14.8% were RII and RIII out of 27 cases tested. In 1995 only one case out of 3 cases tested was at RIII level of resistance. Resistance is high and focal in nature.

KUTCH-BHUJ : With a population of 1.38 million the district is highly endemic with API 3.32 (SPR-2.73, SFR-0.38). The district is having Thar desert with plains and 10% open forest. Resistance at RII and RIII level detected in 1994 was 26.4% out of 53 cases and 29.7 percent out of 37 cases in 1995. The resistance to chloroquine is high and widespread..

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Surat	Utran Kribcho Project	1987	62	39	1	4
		Vanskui	1986	35	17	3	5
2	Panchmahal	Kadana	1993	91	2	17	8
3	Valsad	Lavakar	1995	89	0	6	0
4	Vadodhara	Baroda city	1984	39	1	1	0
			1992	40	0	1	0
		Athadungri	1997	49	0	1	1
5	Amreli	Dhari	1989	33	0	0	0
6	Kheda	Sevalia	1994	34	0	4	4
7	Kutch-Bhuj	Khavada	1994	53	1	8	6
			1995	37	1	8	3

VII.10.HARYANA

The state of Haryana with an area 44212sq.kms supports a population of 19.31 million. The state is located in the northern Plains of India with a rich riverine system. The state has 16 Revenue districts with 397 PHCs. The topography of the state is by and large plain areas with small patch of hill ranges. The entire state is highly irrigated with a vast network of canal system Incidence of malaria is low in the state with an API of 6.64 (SPR-3.98, SFR-0.87). The principal vector in the state is *An.culicifacies*. Population movements within the state are mainly between the urban and rural areas.

The Pf monitoring teams have conducted studies in different districts of Gurgaon, Hissar, Sirsa, Faridabad, Bhiwani, Jind, Rohtak, Karnal and Kurukshetra since 1978. Low levels of resistance (RI) were detected in the districts of Hissar and Sirsa. The districts of Faridabad and Gurgaon have reported both RII and RIII levels although the percentage of RII and RIII cases among the study population was very low.

HISSAR: The district which is irrigated plain land has a population of 2.2 million and reports low incidence of malaria with API 3.09 (SPR-3.86, SFR-0.2). Only RI level of resistance have been recorded in the state in a study conducted in 1986.

SIRSA: This district with a population of 1.0 million reports very low incidence of malaria with API 1.71 (SPR-1.07) which is due to P.vivax. Only RI level of resistance has been detected. Resistance to chloroquine is therefore considered low and focal.

GURGAON: The district with a population of 1.4 million reports high incidence of malaria which are mostly confined to the industrial areas of the district API 15.7 (SPR-6.2, SFR-3.6). The drug resistance studies conducted during 1990, 1994 and 1996 indicated RII and RIII level of resistance.

FARIDABAD: The district with a population of 1.78 million consists mainly of industrial and urban areas with large number of labour population coming from different parts of the country. The incidence of malaria is relatively low with an API 0.75 (SPR-2.69, SFR-0.35). All levels of resistance have been detected only from the industrial complex in 1989. During 1996 only 18.7% cases were at RII level of resistance but the sample size was low. Resistance to chloroquine is high and focal.

SONEPAT: An industrial district with a population of 1.8 million residing on plain irrigated land experiences low malaria endemicity mainly due to P.vivax with an API of 1.71 (SPR-1.07, SFR-0.6). Study carried out in 1980 detected resistance at RI level in all the 11 cases tested. Resistance to chloroquine is considered low and focal.

ROHTAK: The population of the district was 1.8 million mainly depended on agriculture with API 13.13 (SPR-6.94, SFR-0.64). Malaria incidence is on rise. In 1996, one case out of 10 cases tested was at RIII level. Resistance is low and focal.

KARNAL: The district is plain land with high irrigation facilities. The population is 1.14 million with API 12.57 (SPR-3.6, SFR-1.64). In 1994 one RIII case was detected out of 3 cases tested. The resistance is low and focal.

VII.11. JAMMU & KASHMIR

The state with an area of 222236 sq. kms. supports a population of 3.70 million in the two regions of Jammu & Kashmir and is served by 335 PHCs. The Jammu region is situated on the foot hills and has plain land which is mesoendemic for malaria whereas malaria is not reported from the central plateau and higher reaches of Kashmir and Ladhakh. The Jammu region is divided into 8 revenue districts.

Malaria is reported mainly from the districts of Jammu, Kathua, Udampur and Rajouri which are in the foot hills of the sub-himalayan range. In the year 1996 a total of 14487 malaria cases were reported (API-3.9, SPR-3.7) with only 3.7 cases of Pf in the entire state. *An.culicifacies* is the principal vector in the region. Migration takes place on a low scale and malaria transmission is also very low

KATHUA: Drug resistance study in the Jammu region was conducted in the district of Kathua which has a population 0.50 million with API 2.6 (SPR-1.9, SFR-0.02). In-vivo study in 1987 observed a resistant foci at RI level. Since the incidence of Pf. malaria is negligible in the region resistance to chloroquine is considered low and focal.

VII.12.KARNATAKA

The state with a population of 41.5 million occupies an area of 191791 sq.kms. The state has been divided into 20 revenue districts with 1459 Primary Health Centres. It has a long coast along the Arabian Sea and has ecologically two distinct divisions, the Malvador hilly region along the western border and the rest being gently rolling plain land.

The state reported 219198 cases of malaria with 32416 Pf cases (15%) in the year 1996. The API of the state is 5.5 (SPR-2.85, SFR-0.42). The incidence of malaria is mainly confined in the plains in the districts Kolar, Tumkur, Bijapur, Bellary, Gulbadrga, Hassan, Mandya and Mysore. The principal vector is *An.culicifacies*. Migration of and from the fast developing urban/industrialized areas of the state takes place regularly. The Pf monitoring team of NMEP is conducting studies in the state since 1978 but it was only after 1981 that resistance at RI level was detected. The resistance status to chloroquine is generally low though few cases of RII and RIII have been detected in some districts, barring the districts of Kolar, Tumkur and Mysore and in areas of Upper Krishna Project of Gulbarga and Hassan. In all other districts the proportion of RII and RII combined have been less than 15%. Resistance to chloroquine in Pf has not been reported in the districts of Bellary and Belgaum .

TUMKUR: The district with a population of 2.37 million is located in the plains near the city of Bangalore and is moderately endemic for malaria mainly *P.vivax*. About 0.5 million reside in areas with relatively higher proportion of Pf cases. The API of the district is 3.69 (SPR-1.9, SFR-0.11). Resistance at RII level was detected in 1982 only. In subsequent studies RIII cases were also detected. Since less than a quarter of the population is at risk to Pf infection, the distribution of resistance to chloroquine is considered to be low and focal in nature.

MYSORE: The district with a population of 3.31 million has endemicity for malaria although the proportion of Pf cases is static for the last few year. API-3.6 (SPR-2.0, SFR-0.27). The western part of the district fall in the Maland region. Resistance at RI level was detected for the first time in 1981. RII & RIII cases have also been reported in the district. Therefore resistance to chloroquine is low and focal.

CHITRADURGA: The district in the plains with a population of 1.95 million has relatively high endemicity for malaria with API 2.7 (SPR-3, SFR-0.1). RI and RIII level of resistance was detected in 1988. As only 7.7% of the study population showed resistance at RIII level, resistance to chloroquine is considered low and focal.

KOLAR: The district in the eastern plains with a population of 2.30 million comprises of large scale mining projects involving migrating population and is endemic for malaria API-8.7 (SPR-4.7, SFR-1.3). RI and RII levels of resistance have been detected since 1982. In a study conducted in Gulur PHC ,in 1992 48.2% cases were at RII & RIII level and as per the criteria the drug policy has been changed in 1995 in that area. Resistance to chloroquine is considered high and widespread.

BIJAPUR: Situated on the plains with a population of 3.02 million experiences relatively high malaria transmission with API-4.04 (SPR-2.2, SFR-0.9). but has pockets of hyperendemicity. Only one RIII cases have been detected in a study during 1986 in one of the PHC while in other PHC only RI level have been reported and therefore resistance status of chloroquine is low and focal.

RAICHUR: Situated on the plains with a population of 2.4 million having endemicity with API-5.0 (SPR-2.7, SFR-1.0). Studies in 1987 and 1989 detected resistance at RI and RII level but the proportion of cases was less. Resistance to chloroquine is therefore low and focal

GULBARGA: Situated on the plains with a population of 2.63 million and is hypoendemic for malaria with an API of 2.2 (SPR-2.0, SFR-0.5). Resistance detected for the first time by in-vivo in 1985. Though RIII cases were detected in 1987 the proportion of RII and RIII cases were less than 12%. Resistance to chloroquine is considered low and focal.

UKP NARAYANPUR: The Upper Krishna project has a population 0.6 million. The malaria incidence is high with API-64.4 (SPR-10.2, SFR-4.8). Resistance to chloroquine at RII and RIII level detected in 50% of cases tested in sample size of 14 cases. Resistance is considered high but focal.

HASSAN: Situated on the plains with a population of 1.6 million experiences high malaria transmission due to *P.vivax*. The API has been 34.2 (SPR-10.2, SFR-0.6). Only RI and RII level of resistance to chloroquine has been detected in the district and therefore resistance is considered low and focal.

CHICKMANGLUR: Situated in Maland region of western part of the state in the population of 1.02 million is endemic for *P.vivax*. API-13.9 (SPR-5.5, SFR-0.23). Only one case out of 5 cases was at RII level of resistance in the study conducted during 1995. Resistance level is low and focal.

BANGALORE: This metropolitan city with a population of 3.18 million has low endemicity. RI resistance to chloroquine has been detected in a sample of 2 cases. Resistance is considered very low at present.

MANDYA: With a population of 1.65 million having relatively higher endemicity with API 19.7 (SPR-7.1, SFR-0.85). In 1995 though all levels of resistance were

detected, 12.5% of 40 samples tested were at RII and RIII level of resistance. During 1997, only one case of RII was detected in a sample of 10 cases. At present resistance level is low and focal.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Kolar	Gulur	1992	58	21	16	12
2	Gulbarga	Kakkera	1987	34	15	2	2
3	Tamkur	Sira	1982	35	0	5	0
		Gubbi	1983	35	3	3	0
		Chelur	1988	55	29	0	3
4	Bijapur	Konnur	1986	37	24	0	1
5	Chittradurga	Dindiwara	1988	30	20	0	2
6	Mandya	Mahadevapura	1996	40	22	3	2

VII.13.KERALA

The state with an area of 38863 sq.kms. supports a population of 30 million and is situated along the western coast of India on its southern plateau. The state is divided into 14 districts with 959 PHCs. Malaria is of low endemicity as there are reports of indigenous transmission over the few years. API of the state in 1996 was 0.38 (SPR-0.85, SFR-0.05). There is large scale movement of population throughout the year and many imported cases occur originating from different parts of the country.

In the year 1987 one study was conducted in the coastal district of Quilon having 2.5 million population. Malaria incidence is API-0.44. In-vivo resistance study in 1987 observed RI level of resistance.

VII.14.MADHYA PRADESH

A large central state with an area of 443446 sq.kms. supporting a population of 74.84 million is divided into 45 revenue districts having 1376 PHCs. Situated at an altitude varying from 75 to 130 meters has sub-tropical climate with average rainfall of 60 to 160 cms annually. The state borders Uttar Pradesh in the north, Rajasthan in the west, Maharashtra and Andhra Pradesh in the south and Bihar and Orissa in the east.

The state has varied ecological zones with terrain varying from plain to hills covered with forests. The entire state is ridged by the Vindhya ranges running from north to west and the densely forested Satpura ranges running from west to east. The southern part also has the Sahaydari Ranges. The Narmada river traverses the entire state across the centre.

Malaria endemicity of the state is moderately high with an API of 6.7 (SPR-5.12, SFR-2.26). All the districts are not uniformly endemic. The districts in the south east and the western border record higher incidence of *P.falciparum* with the central part relatively free being mostly *P.vivax*. The principal vector is *An.culicifacies*.

Population movement in the state is mostly confined to labour population associated with major irrigation projects. The state also has multiple tourist centres which attract national and international tourists in large scale.

Drug resistance studies are being conducted since 1979. The state as a whole reflects low resistance to chloroquine which are confined to the south eastern parts of the state.

RAIPUR: Situated on the plains in the south eastern part bordering Orissa with a population of 2.3 million is hypoendemic for malaria recording an API of 2.7 (SPR-2.6, SFR-0.0). In-vitro resistance to chloroquine was detected in 1979.

BASTAR: Situated in the extreme south of the state is a large tribal district with a population of 2.57 million and has been divided into two malaria reporting units namely Jagdalpur and Kanker. The entire district is hilly and forested. Malaria transmission is high and perennial with API 9.0 (SPR-3.6, SFR-0.0). The vectors are *An.culicifacies* and *An.fluviatilis*. Migration is restricted to labour population involved in Project works and for exploitation of forest produce. No resistance was detected in a study conducted in 1979. But since, 1980 during the existence of Dandakarayanaya Project, resettlement camps of Bangladesh refugees, resistance to chloroquine in 85% of the study cases were detected at RI level. Apart from this camp area resistance (< 15%) has been observed only in two PHCs. Resistance to chloroquine is low and focal.

MANDLA: A tribal district with a population of 1.5 million is situated in the south central portion of the state on the forested Satpura ranges. Malaria endemicity is high with API 14.34 (SPR-8.8). The district is uniformly endemic with over 40% Pf cases. All levels of chloroquine resistance have been detected by in-vivo studies but in low proportion. Resistance to chloroquine is low and widespread.

JABALPUR: Jabalpur consisting of plain low lands with a population of 3.0 million is situated to the north of Mandla district and experiences low malaria endemicity with API 0.5 (SPR-0.6). In-vitro resistance to chloroquine was detected in 85.7% of the isolates in 1987. In-vivo studies observed that out of 6 cases only two were RI in 1988. During 1990 resistance at RII level was detected but in a lower sample. Therefore, resistance to chloroquine is considered low and focal.

DURG: The district consist of hilly and forest areas and supports a population of 2.71 million with API-8.7 (SPR-7.5). Chloroquine resistance at RII level (6.7%) were detected in 1994 but RII and RIII increased to 13% in 1995 involving two PHCs. Therefore, resistance to chloroquine is low but widespread.

BALAGHAT: A hilly and densely forested district with 70% tribal population bordering Maharashtra in South. Malaria incidence is moderate with API 7.8% (SPR-5.2) and P.falciparum is predominant. Only 3% of cases showed RI level of resistance in a study in 1996. Resistance is low and focal.

BHOPAL: Situated in a undulating plain supporting 2.48 million population with moderately high malaria incidence API 6.33 (SPR-5.0, SFR-1.0). Malaria incidence is high in Bhopal city with high P.falciparum . Resistance to chloroquine at all levels has been detected since 1993. RII and RIII levels were 11.6% and considered high and focal. Sulfa pyrimethamine resistance at RII in low proportion has been detected in Bhopal city during 1994 and 1996.

GUNA: A central district with plains and forested hills is endemic with API 6.93 (SPR-4.4, SFR-1.0) in a population of 1.5 million. The entire district is uniformly endemic. A in-vivo study conducted around a national fertilizer project in 1987 revealed RI level of resistance. Resistance to chloroquine is therefore considered low and focal.

RAJGARH: A predominantly plain district on the foothills with a population of 1.13 million is situated to the south of Guna district experiences relatively high malaria transmission having API 20.22 (SPR-13.7, SFR-0.82). Resistance studies carried out since 1987 have observed RI in a smaller sample size. Resistance to chloroquine is therefore low and focal.

SIDHI: Having a population of 1.6 million has low malaria transmission with API 1.31 (SPR-1.5, SFR-0.31). Terrain is mainly plain with pockets of *P.falciparum* transmission. Only In-vitro resistance to chloroquine was detected in 1980.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Bhopal	Bhopal city	1994	69	2	4	7
			1995	44	1	5	2
			1996	75	2	3	0
2	Durg	Dhamda	1994	30	0	2	0
		Bhimetera	1995	32	0	5	1
3	Balaghat	Paraswada	1996	34	1	0	0
4	Bastar	Pakhanjore	1980	44	2	4	2
		Bhanupratappur	1981	34	2	0	0

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VII.15. MANIPUR

The state with a population of 1.96 million covering an area of 22327 sq.kms situated in the north east part of the country with forested hills and valley. It has 8 revenue districts with 72 PHCs and shares a long border with Myanmar. Population movement across the international border takes place regularly for trade and social reasons.

Malaria incidence as per 1996 data in the state is low with an API of 1.1 (SPR-1.94, SFR-0.84). The districts of Churachandpur, Tamenglong and Chandel are the main malarious areas. The principal vector is *An.minimus* supported by *An.dirus* and *An.fluviatilis*.

Drug resistance study conducted in 1981 detected RI and RII levels of resistance and in 1994 all levels of resistance were reported. Although the sample size was small resistance to chloroquine is considered high but focal in distribution.

CENTRAL DISTRICT: A hilly forested district with a population of 0.72 million records API of 1.45 (SPR-3.82, SFR-2.3) but there are pockets of high malaria transmission. Studies conducted in Jiribam area reported RI & RII level of resistance in low proportion. Resistance to chloroquine is therefore low and focal in distribution.

CHANDEL: hilly forested district bordering Myanmar with a population of 0.8 million. Large scale inter country movement for trade, socio economic, and cultural reasons takes place. The API was 0.59 (SPR-1.23, SFR-0.13). Malaria is of low endemicity. In a study conducted in 1994 16.7% were at RII and RIII level resistance in a sample size of 24 cases. Resistance is considered high and focal.

SENAPATI: A hilly district with dense forest and narrow valleys. The 0.23 million population primarily depend on agriculture, jhum cultivation and on forest produces. An endemic district with API 0.7 (SPR-1.34, SFR-0.13). RI level of resistance to chloroquine was detected in 1994 in one case out of five tested. Resistance to chloroquine is considered low and focal.

VII.16. MAHARASHTRA

Maharashtra is a large state with an area of 307690 sq.kms. It has a population of 88.33 million and is divided into 30 revenue districts with 1695 PHCs. The state has varied eco-systems ranging from coastal and plain areas to hilly forested areas. The forested and hilly areas of the state along its northern and eastern parts are contiguous with the eco-systems of Andhra Pradesh and Madhya Pradesh inhabited mainly by tribal populations.

Malaria incidence of the state is not uniform and is focal in nature. The API of the state is 3.59 (SPR-2.38, SFR-0.63). The districts of Raigadh, Thane, Dhule, Jalgaon, Ahmed Nagar and Aurangabad in the western and northern part of the state are moderately

endemic whereas the districts of Yeotmal, Chandrapur, Bhandara and Gadchiroli bordering Madhya Pradesh in the east and Andhra Pradesh in the south and Nasik bordering Gujarat in the north are hyperendemic with Pf predominance.

Migration across the border with Andhra Pradesh and Madhya Pradesh is confined among the tribal populations in the districts of Chandrapur and Gadchiroli and is due to socio-economic pressures.

The principal vector in the state is *An.culicifacies* supported by *An.fluviatilis* in the hilly and foothill areas. Drug resistance studies have been conducted since 1978 in the districts of Chandrapur, Thane, Gadchiroli, Bombay, Pune, Raigadh, Nasik and Bhandara. RI and RII levels have been detected in all districts except Bhandara. Only in Raigadh and New Bombay RII & RIII cases against chloroquine were detected. Revised drug policy (1995) with second line of treatment i.e sulfa-pyrimehamine is being followed in Washi PHC of Raigadh district.

CHANDRAPUR: The district with a population of 1.98 million consists of plain as well as hilly and forested regions. The API of the district was 12.33 (SPR-4.73, SFR-0.67). Studies have been conducted since 1978. Resistance at RI and RII levels have been detected apart from in-vitro resistance. Revised drug policy is being followed in the area since 1981. Resistance to chloroquine is considered as low and widespread.

PUNE; The district with a population of 4.4 million was low endemicity for malaria with an API of 1.89 (SPR-1.56, SFR-0.41). Malaria is mainly confined to the hilly and forested areas of the district. Studies in 1983 have detected in-vitro resistance to chloroquine. Although RII (28.6%) cases were detected in 1992, the study sample was small (7) and therefore resistance to chloroquine is considered low and focal.

THANE: The district on the western coast and foothills with a population of 5.9 million is highly endemic for malaria API-7.35 (SPR-5.46, SFR-2.02). Two studies have been conducted. RI level of resistance has been reported in 1980 and 1981. Resistance to chloroquine is low and focal.

NEW BOMBAY: The district on the western coast is mainly urban with a population of 11.12 million and is endemic API-2.2 (SPR-3.69, SFR-0.55). *P.vivax* is predominant. RII & RIII levels of resistance have been reported in 1991 and 1996 from a developing area of the city . Resistance to chloroquine is considered low but focal.

RAIGADH; A coastal district with a population of 2.04 million is hyperendemic with API 4.74 (SPR-3.35, SFR-1.24). The district is along the foothills of the western ghats. One study conducted in 1991 detected RII and RIII cases (35%) in 31 cases. Resistance to chloroquine is considered high and widespread. Revised drug policy (1995) has been introduced in Washi PHC following this study.

NASIK: The district bordering Gujarat in North-West having a population of 4.31 million is a hilly and forested district with hyperendemicity API-8.4 (SPR-4.44, SFR-1.26). The entire tribal population is at risk of P.falciparùm malaria. In a study conducted in 1995, low proportion of RII level of resistance (4.41%) was detected. Presently resistance status is low and focal.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Chandrapur	Yetapalli	1979	47	9	4	0
		Gadchandura	1978	32	2	0	0
2	Raigarh	Washi	1991	31	0	6	5
3	Nasik	Surguna	1995	45	0	2	0

VII.17.MEGHALAYA

A north-eastern state with a population of 1.95 million covers an area of 22429 sq.kms. and is divided into 4 revenue districts with 88 PHCs. The state shares a long international border with Bangladesh. The state is predominantly hilly and forested with heavy rainfall. Malaria incidence of the state is high with API of 13.29 (SPR-8.5, SFR-4.3) as per 1996 epidemiological data. More than 50% of the total malaria cases are due to Pf. The principal vector in the state is *An.minimus* supported by *An.dirus* and *An.fluviatilis*. All the 4 districts are highly endemic for malaria. The resistance at all levels to chloroquine has been detected in the state. Due to high resistance revised drug policy is followed in all the district of the state except Jaintia Hills since 1983.

GARO HILLS: A hill forested district with a population of 0.74 million is highly malarious with an API of 10.5 (SPR 4.85, SFR-4.8). The entire population is at risk of Pf infection. Resistance studies conducted since 1979 showed resistance at all levels. An increasing trend in the degree of resistance was observed since 1990. Resistance to chloroquine is considered high and widespread. In-vivo resistance to sulfa-pyrimethamine (2 tabs stat) at RI (14.3%) was reported in 1979 but was not observed in subsequent studies in 1991 and 1992.

KHASI HILLS: The entire population of 0.96 million residing in hilly forested areas having an API OF 7.6 (SPR-7.8, SFR 4.7) at risk of malaria. Studies conducted since 1980 recorded all levels of resistance but study sample was very small. Resistance is considered low and widespread.

JANTIA HILLS: A hilly forested district with a population of 0.3 million is highly malarious with API of 42.6 (SPR-20.7, SFR-1.81). The entire population is at risk. RII level of resistance to chloroquine has been detected in 1995 in two cases out of 17 cases tested. Resistance level is considered low and focal at present.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	W.Garo Hills	Zikzak	1990	32	0	5	3

VII.18.MIZORAM

A north-eastern state bordering Myanmar has an area of 21031 sq.kms. and supports a population of 0.72 million. It consists of 4 revenue districts with 38 PHCs. The entire state is ridged with hills and forests. Malaria incidence is very high with API of 15.2 (SPR-5.3, SFR-3.0). Transmission is very intense in all the districts with predominantly P.falciparum . The principal vector is *An.minimus* supported by *An.dirus* and *An.fluviatilis*. Inter-country movements across the borders of Myanmar is a regular feature. Pf monitoring teams of NMEP conducted drug sensitivity studies with chloroquine, sulfa-pyrimethamine and quinine since 1981 in the districts of Aizwal and Lunglei and resistance at all levels have been detected with chloroquine. Resistance to chloroquine has been gradually increasing in frequency and degree.

In 1991 the drug policy for two PHCs in Aizwal and Lunglei district have changed and the 2nd line of treatment with sulfa-pyrimethamine is being followed for all fever cases.

AIZWAL(WEST) Population is 0.29 million and the entire population is at risk of malaria. The terrain is hilly and forested. Malaria transmission is intense with an API of 16.84 (SPR-6.1, SFR-4.2). Studies carried out since 1981 detected increasing levels of resistance. In Sairang PHC in 1981 resistance upto RIII level was detected. In 1997 all the cases of 8 samples tested were S/RI .

In-vivo resistance to sulfa pyrimethamine at RI level was detected in 1983 and 1988 respectively.

LUNGLEI: A hilly forested district with a population of 0.11 million experiences intense malaria transmission with an API of 29.41 (SPR-7.65, SFR-3.8). Studies conducted since 1983 reveal an increasing trend in frequency and level of resistance to chloroquine. In a PHC in 1983 RI and RII levels were detected in 16.7% of cases with no RIII but in the same PHC in 1989, 33.3% of 24 cases were at RIII level. Resistance to chloroquine is high and widespread. Second line of treatment has been introduced in the PHC since 1991. Comparative in-vivo study with chloroquine and amodiaquine indicated no significant difference in the response rate.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Aizwal	Sairang	1981	47	19	8	1

VII.19.NAGALAND

A north-eastern state bordering Myanmar covers an area of 16579 sq.kms. with a population of 1.34 million and consists of 7 revenue districts with 33 PHCs. The terrain is hilly and forested. Inter country movements across the border of Myanmar is a regular feature.

Malaria incidence is moderate with API 1.01 (SPR-4.67, SFR-1.73) as per 1996 information. All the districts except Phek district records high incidence with about 32% of Pf. The principal vector is An.minimus supported by *An.dirus* and *An.fluviatilis*.

Drug resistance studies so far conducted in the districts of Kohima, Mon and Mokakachung recorded resistance to chloroquine both by In-vivo and In-vitro studies. Revised drug policy is being followed in whole of the state since 1981.

KOHIMA: A hilly forested district and the entire population of 0.5 million is at risk of malaria experiencing an API of 2.1 (SPR-7.5, SFR-1.2). Studies conducted since 1978 detected all levels of resistance with high proportion of RII and RIII cases. Resistance to chloroquine is high and widespread in distribution.

MON: A hilly forested district with a population of 0.18 million which is uniformly hyperendemic for malaria. API of the district is 3.85 (SPR-6.3, SFR-1.44). A study conducted in 1989 recorded a case of RIII in a study population of two. Resistance to chloroquine is suspected to be high and widespread.

MOKOKCHUNG: A population of 0.2 million reside in this hilly forested and hyperendemic district recording an API of 4.08 (SPR-7.7, SFR-1.2). Only one in-vitro study was conducted in 1978 which recorded resistance to chloroquine. Though Pf transmission is low it is suspected to be resistant to chloroquine.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Kohima	Dimapur	1984	34	9	1	0

VII.20.ORISSA

Orissa covers an area of 155707 sq.kms. supporting a population of 34.54 million. It has four distinct ecotypes viz. the northern plateau, the eastern ghat region, the central tract and the coastal plains. It has 30 revenue districts with 1056 Primary health centres. Apart from the three coastal districts the rest of the 27 districts are forested foot hills and hills. Malaria incidence in the state as a whole is high with API 13.30 (SPR-11.8, SFR-10.22) as per 1996 data. Except for the three coastal districts all the other districts experience high malaria transmission which is relatively stable. The vectors are *An.fluviatilis, An.varuna, An.minimus* and *An.annualris* with *An.culicifacies* in certain

parts.

Movement out of the state generally of labour population to various parts of the country especially to the northeast region is high and frequent.

Resistance studies are being carried out since 1978 and till date most of the districts have been repeatedly studied. RI cases were detected in the initial studies and after 1985 all levels of resistance cases were detected. Though most studies indicated a fair proportion of the sample being resistant, RII and RIII levels of resistance never exceeded more than 25%. In-vitro studies conducted in all districts except Kalahandi revealed resistance to chloroquine. Resistance to chloroquine is gradually increasing and is widespread.

PHULBANI: Situated in the eastern ghats with a population of 0.60 million. About 70% of population is residing in high Pf areas in 13 PHCs which are hilly and forested. Malaria transmission is intense and perennial with API 48.0 (SPR-18.6, SFR-18.0). Resistance at RI level was first detected in 1978 and subsequent studies revealed gradually increasing resistance at all levels though combined RII and RIII has been 10.4% and therefore resistance to chloroquine is considered at low level but widespread.

BOLANGIR: Situated on the central tract with a population of 1.34 million. Terrain is hilly and forested. Malaria incidence is high with API 13.8 (SPR-10.27, SFR-7.4). Resistance to chloroquine is low and focal as only 1 out of three studies since 1980 detected 8.9% of RI cases only.

DHENAKANL: Situated on the central tract with a population of 1.05 million of which 10% reside in hilly forested areas experiencing intense Pf transmission. Malaria incidence in the district is high with API 22.5 (SPR-18.4, SFR-13.7). In-vivo resistance at RI and RII levels were detected in 1982 and thereafter all levels of resistance were reported but the proportion of RII and RIII were low. Resistance to chloroquine is therefore low and widespread.

CUTTACK: A coastal district with a population of 2.18 million. Malaria incidence is low API-1.5 (SPR-2.66, SFR-1.92) except in pockets bordering Ganjam district. In-vitro resistance was present but in-vivo study detected only 2 (14.3%) cases at RII level in a low sample size. Resistance to chloroquine is low and focal.

KORAPUT: Situated in the eastern ghats with a population of 1.13 million with 45% at risk of high risk of Pf malaria. The district has been divided into three new districts. The ecology is mostly forested and hilly. the malaria incidence is high with API 20.4 (SPR- 14.44, SFR-14.12). Resistance studies in Malkangiri PHC in 1982 out of 35 cases only 1 case of RI was detected. Recent study of 1993 also indicated RIII resistance 12.5% out of 8 cases studied. The resistance status in other areas of study was generally low hence resistance to chloroquine is low and widespread.

GANJAM: Situated in the eastern ghats with a population of 3 million. Most of the population is living in the forested and foothill areas. The malaria incidence is high

with API of 5.0 (SPR_7.9, SFR-6.6) and is mainly confined to 7 PHCs. Resistance studies since 1979 have indicated a low level of in-vivo resistance. Resistance to chloroquine is low and focal.

KEONJHAR: Situated in the northern plateau with a population of 1.48 million of which 75% reside in hilly and forested areas with high risk of Pf infection. The malaria incidence is high with API of 39.01 (SPR-16.7, SFR-16.4). Resistance studies during 1979 and 1983 reported RI cases in very low proportion But in 1987 the presence of RII and RIII cases were noted in less than 15% of the 21 cases tested. Thus the resistance to chloroquine is low but widespread.

KALAHANDI: Situated in the eastern ghats with a population of 1.25 million of which about 60% is at high risk of Pf malaria. The terrain is mostly hilly. The API has been constantly high with API-11.0 (SPR-11.5, SFR-9.2). The resistance study in 1986 in Jaipatna PHC detected RI level of resistance only. Resistance to chloroquine is low and focal.

MAYURBHANJ: Situated in the northern plateau with a population of 2.04 million with the entire population at high risk of malaria. Malaria incidence in this hilly forested district is high with API of 23.42 (SPR-15.08, SFR-13.9). Resistance studies since 1983 have consistently demonstrated the presence of RI cases but in low proportion but in the study during 1991 did not detect any resistance. Resistance to chloroquine is low and focal.

SUNDERGARH: Population of 1.74 million living in plains and forested foothill areas with high Pf transmission. Malaria transmission is intense with API of 32.0 (SPR-14.2, SFR-13.3). Resistance studies in 1984 and 1993 detected RII and RIII in low sample size.. Resistance to chloroquine is therefore low but widespread.

SAMBALPUR: Situated in the central tract with a population of 0.9 million with nearly 50% residing in high Pf transmission areas. The undulating plains and foothills of the district experience intense malaria with API 16.8 (SPR-9.4, SFR-8.6). Though RI and RII cases were detected in 1984 in low proportion it had markedly increased by 1986 to 46.5% of RI and 11.6% of RII in 43 cases studied. Therefore resistance to chloroquine though increasing is considered low and widespread.

BALASORE: A coastal district with a population of 1.9 million of which only 6% is living in high Pf transmission areas. Malaria transmission is relatively low with API 3.4 (SPR-3.9, SFR-3.1) . In-vitro resistance study indicated resistance in 1984 but in-vivo study observed only RI level of resistance. Resistance to chloroquine is therefore low and

focal

PURI: A coastal district with a population of 1.44 million experience low malaria transmission with API 0.72 (SPR- 1.52, SFR-0.14). it is a tourist district. Two in-vivo resistance studies were conducted in 1983 and 1988. Though RI cases (11.1%) were detected in the earlier study the later study revealed RI and RII cases in a low sample size of 8 cases. Resistance to chloroquine is low and focal.

RAYAGADA: A newly created district with hilly and forested bordering with Andhra Pradesh. The population of the district is 0.79 million experiences high and intense malaria with Pf predominant API 21.82 (SPR-14.7, SFR-13.9). Resistance studies conducted in 1994 detected RI and RII 1in 6.7% of 30 cases but in 1995, RII and RIII level detected in 8.4% of 83 cases indicating rise in resistance level. Presently resistant is at lower level and focal in nature.

NAUPADA: A newly created district situated in extreme West bordering with Madhya Pradesh with a population of 0.52 million. This hilly and forest district experiences intense malaria with Pf predominant API 24.7 (SPR-15.22, SFR-19.2). Resistance study conducted in 1996 detected 10.5% cases of RII and RIII in a population of 38 cases tested. Resistance is considered low and focal.

BOUDH: This hilly and forested district recently created from the district Phulbani having a population of 0.35 million with Pf predominant API-8.4 (SPR-10.7, SFR-7.5) All level of resistance detected in a study in 1997, RII and RIII being 13.04%. The resistance level is on higher side but focal.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Phulbani	Gumagarh	1978	52	2	0	0
			1979	34	3	0	0
			1993	34	2	4	2
			1996	34	0	0	0
		Khajuripada	1985	35	3	3	0
		Raikia	1996	32	1	3	0
2	Boudh	Adanigarh	1997	46	1	5	1
3	Naupada	Khadial	1996	38	0	3	1
4	Bolangir	Khaprakhol	1980	45	4	0	0
5	Dhenkanal	Bantala	1982	35	9	3	0
		Khania	1990	33	1	1	3
		Khajurikata	1989	40	2	1	2
6	Malkangiri	Malkangiri DNK	1982	35	1	0	0
7	Keonjhar	Padmapur	1988	32	23	1	1
		Telkoi	1985	50	0	5	0
8	Mayurbhanj	Kaptipada	1983	31	6	0	0
9	Sambalpur	Garposh	1984	42	1	2	0
		Fasimal	1986	43	20	5	0
10	Rayagada	Kashipur	1994	30	1	4	0
			1995	83	0	6	1
11	Gajapati	R.Udaigiri	1996	46	0	2	1

VII.21.PUNJAB

A north-western state bordering Pakistan has a population of 22.7 million with an area of 50362 sq.kms. and is divided into 12 revenue districts with 484 Primary Health Centres. The terrain of the state is mainly plain with largely irrigated areas. The state attracts large number of labour populations from different parts of the country for agricultural purposes. Incidence of malaria in the state is low with an API of 1.2 (SPR-1.10, (SFR-0.01) and P.falciparum incidence is insignificant. Malaria incidence is confined mainly to the districts of Patiala, Ropar and Sangrur. The principal vector is *An.culicifacies*.In-vivo resistance studies with chloroquine detected few RII cases in the district of Patiala only.

PATIALA: Situated in the sub-montane region with a population of 1.7 million and experiences low Pf infection. API of the district is 4.47 (SPR-2.9, SFR-0.6). Resistance study conducted in 1985 detected resistance at RII level among 3 cases studied therefore resistance to chloroquine is considered low and focal.

SANGRUR: Situated in the plain areas with a population of 1.9 million. Malaria endemicity is relatively low with API of 1.9 (SPR-1.50, SFR-0.61) and is predominantly due to P.vivax. Resistance to chloroquine has been detected by in-vitro studies in 1985.

VII.22.RAJASTHAN

The state with a population of 44.01 million occupies an area of 342239 sq.kms. and has in addition to plain areas forests in the southern and desert in the western part. It has been divided into 31 revenue districts with 1572 PHCs. Incidence of malaria is significant in the Thar desert area. Hilly forested areas along the eastern border of the state support large number of tribal population.

Malaria incidence of the state is high and is mainly confined to the desert and forested areas (API-6.83, SPR-4.6, SFR-1.10) as per 1996 data. The incidence is particularly high in the western and southern districts. Principal vectors in the state are *An.culicifacies* and *An.stephensi*, the latter playing a significant role in the desert area.

Migration takes place mainly involving labour populations for construction activities and also across the forested areas of eastern side for socio-economic reasons. Studies conducted since 1980 have detected chloroquine resistance in 18 districts so far.

Resistance to chloroquine has been detected in all the districts studied with varying degrees. There is a definite increase in the proportion of resistance cases though the

RII and RIII proportion is less. The state as a whole has low resistance to chloroquine with an increasing trend.

BHARATPUR: With a population of 1.7 million residing in plain areas experience high endemicity with API 44.74 (SPR-13.5, SFR-6.7). Malaria transmission is confined to less than 25% of the population. In-vitro study detected resistance in 1980 but not in simultaneously carried out in-vivo study. Study in 1984 detected only 3% of 33 cases at RI level. Resistance to chloroquine at RIII level was detected in 1996 only . Resistance to chloroquine is low and focal.

KOTA: Situated in the south-eastern part bordering Guna of Madhya Pradesh has a population of 1.22 million with moderate risk to malaria (API-6.21, SPR-4.6, SFR-2.30). The terrain which is plain and forested land support 39% of the population and also experience high Pf infection. Resistance studied carried since 1988 have consistently detected high RI but low RII and RIII in Morak PHC in which a thermal power project is situated. All the 32 cases tested were susceptible in a study conducted during 1996. Resistance to chloroquine is low and focal.

CHITTORGARH: A small district in the south-eastern part bordering Madhya Pradesh consists of plain land with forest in parts and supports 1.5 million population. Malaria endemicity of the district as a whole is moderate with API 9.5 (SPR-7.9, SFR-4.0). A single study carried out in 1989 indicated RI and RII cases in a low proportion. Resistance to chloroquine is low and focal.

BUNDI: A south-eastern district which is hilly and forested has a population of 0.77 million. On the whole it experiences high malaria transmission with API 12.9 (SPR-9.34, SFR-4.67). Resistance studies carried out in 1990 detected resistance at RI and RII but in 1992 RIII level was also detected. Resistance to chloroquine is therefore considered low and widespread.

BIKANER: A large desert district with a population of 1.21 million. Malaria incidence as a whole in the district is moderate with API of 8.0 (SPR-6.4, SFR-3.2) but there are pockets of high malaria incidence. There is transitory movement of tourists in the district. Studies conducted in 1992 and 1995 revealed low and focal resistance to chloroquine.

JALORE: A district in the plain having a population of 1.14 million of which 24% reside in high Pf incidence areas. Malaria incidence is low with API of 2.6 (SPR-2.7), SFR-1.4). Resistance study carried out in 1993 detected RII (11.45%) cases and therefore resistance to chloroquine is low and focal.

DUNGARPUR: Population is 0.88 million with 78% residing in high Pf areas. The topography is mostly plains and forested foothills with natural water reservoirs. Malaria transmission is high with API 14.6 (SPR-8.4, SFR-4.2). There is inter and intra state population movement for socio-economic reasons. Resistance studies carried out since 1987 detected all levels of resistance with more than 20% of RII and RIII cases.

Therefore resistance to chloroquine is high and widespread.

BANSWARA: A district on the plains and foothills has a population of 1.16 million. about 0.7 million reside in highly malarious areas. The API of the district is 2.63 (SPR-1.66, SFR-0.83). Interstate movement of tribal population is a regular feature. The resistance studies conducted since 1986 detected all levels of resistance and the proportion of RII and RIII have been less than 20%. In-vitro resistance was also detected. Resistance to chloroquine is considered low and widespread.

UDAIPUR: The district with a population of 2.10 million is situated on the plains and foothills. Malaria endemicity is moderate with an API of 5.9 (SPR-5.62, SFR-2.5). The district attracts large number of tourists throughout the year. Studies conducted since 1987 detected all levels of resistance although mostly of RI level but in a low sample. Resistance to chloroquine is therefore low and widespread.

BARMER: The terrain is mainly desert with a population of 1.44 million of which 40% reside in highly malarious areas. The district is highly endemic for malaria recording an API of 7.5 (SPR-5.7, SFR-2.8). Studies conducted so far detected RI (77%) cases although stray cases of RII and RIII level were also reported. Resistance to chloroquine is high and widespread.

JODHPUR: Another desert district with a population of 2.2 million. API of the district is 3.4 (SPR-3.5, SFR-1.7). There is large and regular influx of tourists. The resistance study conducted in one of the PHC detected only RII level of resistance. Resistance to chloroquine is low and focal.

SIROHI: About 50% of the total population of 0.65 million reside in highly malarious areas. Terrain is mostly plains and foothills. API of the district is 3.6 (SPR-3.2, SFR-1.6). Study conducted in 1991 detected high proportion of RI level but RII and RIII proportion was low. Resistance to chloroquine is considered low and widespread.

JAISALMER: Population is 0.35 million with 18% living in highly malarious areas . Terrain is mostly desert attracting large number of tourists. API of the district is 25.7 (SPR-11.8, SFR 9.0). Studies carried out since 1992 detected RI and RII level of resistance. Resistance to chloroquine is therefore low and focal.

BHILWARA: Population is 2.15 with movement of labourers both inter and intra state in this district. Malaria transmission is high with API 15.7 (SPR-12.7, SFR-6.4). Resistance at RI level was detected in one PHC but in a low sample size. Resistance is low and focal.

PALI: In a population of 1.49 million API 3.9 (SPR-3.1, SFR-1.5). RI and RII level of resistance to chloroquine was detected. RII being 10.3% of 29 cases tested in a PHC in 1995. Resistance is low and focal.

ALWAR: This district is with population of 2.3 million having industrial set up which draws large labour force both from outside and within the state. The Principal vector is *An.culicifacies*. Resistance study in 1997 detected 7.5% RII and RIII level of resistance and therefore considered low and focal.

DHOLPUR: A south eastern district which is hilly and forested has a population of 0.75 million. Malaria incidence is moderate with API-6.22 (SPR-2.9, SFR-1.5). Resistance studies conducted during 1996 detected all levels of resistance to chloroquine but in 1997 only RI level of resistance was detected. Resistance is low and focal.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Bharatpur	Roopbas	1980	30	0	0	0
			1984	33	1	0	0
		Deeg	1996	46	20	0	1
2	Bundi	Kapran	1992	36	12	0	6
3	Jalore	Ahore	1993	35	18	4	0
4	Dungarpur	Bicchiwara	1993	35	1	4	4
5	Dholpur	Basainawab	1996	31	13	2	6
6	Barmer	Baitu	1990	59	38	2	4
			1992	33	1	2	1
7	Jodhpur	Salwas	1994	30	0	5	0
8	Jaisalmer	Pokhran	1995	35	15	1	0
9	Swaimadhopur	Masalpur	1995	43	1	2	6
10	Alwar	Gobindgarh	1997	40	22	1	2
11	Kota	Morak	1993	31	0	2	4
			1996	32	0	0	0

VII.23. TAMIL NADU

A coastal state on the eastern shore has an area of 130058 sq.kms. and supports a population of 60.77 million. Malaria transmission is low and largely confined to the coastal districts of Madras and Ramanatha Puram. API of the state is 1.0 (SPR-1.12, SFR-0.05) as per 1996 epidemiological data. Large scale population movements take place in these two districts. The terrain is coastal and plain with hills on the western borders. Principal vectors are *An.stephensi* and *An.culicifacies*. The state is divided into 45 districts and has 1436 PHCs.

Resistance studies were conducted in the districts of Ramanatha Puram and Chennai. In Ramanatha Puram study carried out during 1979 did not detect any resistance but studies conducted in Chennai city since 1984 showed the presence of gradually increasing levels of resistance.

CHENNAI: A coastal district with a population of 4.15 million with an API of 9.27 (SPR-11.48, SFR-0.25) but majority of cases are reported from the city. Resistance studies carried out in Chennai city indicated that the level of resistance has been gradually increasing since 1984. In 1984 there was only 1 case of RI out of 31 cases studied apart from in-vitro resistance to chloroquine. But in 1992 and 1993 all levels of resistance were detected. At present resistance to chloroquine in Chennai city is considered high and focal.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Chennai	Chennai city	1984	31	1	0	0
			1992	31	13	8	5

VII.24.TRIPURA

A north-eastern state with an area of 10486 sq.kms.supports a population of 3.1 million. It share a long border with Bangladesh being surrounded by it from three sides. It is divided into 3 revenue districts and has 63 PHCs. The terrain is hilly and forested and large scale movements of population takes place across the international border.

Malaria incidence is high with an API of 3.2 (SPR-4.45, SFR-3.2). The incidence is mainly confined to North and south Tripura district. The principal vector is *An.minimus* and plausibly supported by *An.dirus* and *An.fluviatilis*.

Chloroquine resistance studies conducted in south Tripura district since 1981 detected all levels of resistance but in low frequency and no significant difference in the resistance status was observed in 1988.

SOUTH TRIPURA: A hilly forested district with the entire population of 0.82 million at high risk of Pf malaria, records an API of 5.14 (SPR-7.35, SFR-5.51). The resistance studies carried out in 1981 detected RI and RII levels of resistance in low proportion. RIII level of resistance to chloroquine was detected in 1988 and 1993 but the sample size was low. Therefore resistance to chloroquine is presently high and widespread.

Resistance to sulfa-pyrimethamine combination was observed at RI level in 3.2% of 31 cases studied in 1993.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	S.Tripura	Santirbazar	1981	33	10	2	0

VII.25.UTTAR PRADESH

A large state with an area of 294411 sq. km divided into 62 revenue districts with 3761 PHCs. The state share a long border with Nepal in the north and has a population of 126.5 million. The state is predominantly plain land with only the north western district being hilly. Malaria endemicity of the state as a whole is relatively low with API 1.34 (SPR-1.83, SFR-0.23). Only 14 districts have recorded more than 2 SPR in the past years. Majority of these districts are confined to central plain and northern hilly areas. Risk of Pf infection is relatively low never exceeding 30% in most of the districts. The principal vector is *An.culicifacies* with *An.fluviatilis* in the foothills. In-vivo resistance studies conducted since 1978 has detected resistance to chloroquine in 8 districts. Resistance in some districts were detected as early as 1980 at RII level and though there have been little increase in proportion of resistant cases but the degree has not significantly changed. Resistance to chloroquine in the state as a whole is low and focal.

MATHURA: With a population of 2.1 million, is situated to the west to Delhi and had recorded in-vitro resistance to chloroquine as early as 1979. The district is famous for pilgrimage and also has few Industrial projects. Malaria endemicity is low with API 1.9 (SPR 1.7 : SFR 0.7). Subsequent resistance study in 1981 detected 13.3% RI and RII resistance in a sample of 15 cases with chloroquine in the area. Resistance therefore is low and focal.

MEERUT: Situated on the western irrigated plains of the state with a population of 3.23 million experience low transmission with API 0.13 (SPR-0.2, SFR 0.1), In-vivo study in 1986 detected RI level of resistance. Resistance to chloroquine is low and focal.

NAINITAL: Situated on the sub-Himalayan foothills in the northern part of the state has a population of 1.6 million. Malaria transmission is low with API 1.02 (SPR-1.32 SFR 0.04). About 2% of the population is at risk of Pf Malaria. Migration is restricted among the tourists. Study in 1983 and 1986 indicated RI level of resistance. Resistance to chloroquine is considered low and focal.

PILIBHIT : Small district with a population of 1.39 million is situated on the sub-Himalayan foothills in the northern part of the state and borders Nepal in the east. Malaria transmission is low with API 0.08 (SPR 0.1 SFR 0.02). In-vivo study in 1988 observed RI and RII resistance with only 13.3% at RII level. Resistance to chloroquine is therefore considered low and focal.

KHERI : Situated on the foothills of the sub-Himalayan ranges borders Nepal and has a population of 2.6 million. The district experience low malaria transmission with API 0.3 (SPR - 0.5, SFR 0.3). Study in 1987 detected RI level of resistance. Resistance to

chloroquine is low and focal.

ALLAHABAD : With a population of 4.2 million is situated on the Indo-Gangetic plains in the southern region of U.P. transverse by the Yamuna and Ganges Rivers. Malaria transmission is low with API 1.82 (SFR 3.0, SFR 0.41). In-vivo studies conducted in 1986 detected RI level of resistance. But in subsequent studies RII level of resistance was also detected but in a lower sample size. Similar observations were made by other institutions. Repeat study in one of the PHC reported sensitivity in P. falciparum. Resistance to chloroquine is considered low and focal.

MIRZAPUR : Located to the west of Allahabad with 1.87 million population consists of plains irrigated land. Malaria endemicity is moderately high with API 6.7 (SPR 6.3). In-vivo study in 1979 detected no resistance but in subsequent studies RI and RII cases were detected but in low proportion. Resistance to chloroquine is considered low and focal.

SONBHADRA : Situated in Indo-Gigentic plain in southern Part of the State having a population of 1.24 million with high malaria incidence API 27.1 (SPR 25.9, SFR 1.0). RI and RII level of resistance in 4.1% cases of 49 samples was detected in 1994. Resistance to chloroquine is low and focal.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Mirzapur	Muirpur	1979	36	0	0	0
2	Sonbhadra	Muirpur	1994	49	1	1	0

VII.26. WEST BENGAL

The state of West Bengal situated in the east with and area of 88752 sq. kms. borders Bangladesh in the east and Bay of Bengal in the south. The state also borders in the north Bhutan and Nepal in the north west. The entire state has 17 revenue districts and 1556 PHCs serving a total population of 104.6 million. The entire state is plain land with hills, tea gardens and forests fringes confined to the northern districts. The Malaria vectors in the plains are mainly *An. culicifacies, An.philippinesis* and *An.stephensi* with *An.minimus* in the foot hill district.

Malaria endemicity in the state as a whole is low with API 0.9 (SPR 3.8 SFR 0.9). Malaria transmission is not uniform in all districts and only 5 district namely Calcutta, Jalpaiguri, Darjeeling, Coach-Behar and Purulia record SPR 1.5 to 25.5. All these five districts have Pf transmission that is more than 15% to 83% of total malaria cases. Except for Purulia which is situated in the western part of the state bordering Bihar and Orissa the other four malarious districts are situated in the north and in south, the Calcutta Municipal Corporation.

In-vivo studies have been conducted since 1981 in six districts. Resistance to chloroquine at all levels were detected in the early part of the 80's but largely confined to RI level but is observed to be gradually increasing in frequency and degree over the years. Resistance to chloroquine is therefore considered high and focal being confined to only 5 districts. Revised drug policy (1995) has been introduced in Ajudhya hill and Uttarlatabari PHCs of Purulia and Jalpaiguri districts respectively.

PURULIA : Situated in the western part of the state with population of 2.1 million. The terrain is generally plain with forested hills in the periphery. Malaria transmission is moderate with API 2.9 (SPR 4.2 : SFR 0.79). The entire district does not experience malaria transmission uniformly and only 15% of the population is at risk of Pf malaria. Resistance studies carried out in 1981 detected 32% at RI level and only 10% at RII and RIII level. Later studies in 1992-95 indicated 25.5% of the cases at RII and RIII level indicating an increase in the degree of resistance and stabilization. Although RII and RIII level of resistance were not reported during 1996 but during 1997 again resistance at all level have been reported. Resistance to chloroquine is therefore considered high and widespread. RIII resistance to sulfa-pyrimethamine was detected in a single case (3.4%) in 29 cases tested.

JALPAIGURI : Bordering Bhutan in the north and Bangladesh in the south is entirely covered with forest ranges. Though the entire population of 2.59 million experience uniformly high malaria endemicity having API 9.34 (SPR-13.6, SFR 3.02) transmission is particularly intense in the tea estate. In-vivo studies carried out in 1982 detected 45% resistant at all levels with only 9.1% RII and RIII level but in 1990 34% RIII cases were detected. Subsequent studies detected 11% of RII and RIII levels of resistance in the district. Resistance to chloroquine which has considerably increased is considered high and widespread.

In-vivo resistance to sulfa-pyrimethamine was detected in 1994 at RI level.

COOCH-BEHAR : This district bordering Bangladesh is predominantly hilly with forest fringes. With population of 2.22 million it experiences moderate malaria transmission with more than 20% P.falciparum cases (API 1.6 : SPR 3.8 SFR 0.9). Two in-vivo studies were carried out in 1989 and 1991 with only 4 and 9 cases respectively. RIII resistance have been reported but in a lower sample size. Resistance to chloroquine is considered low and focal.

MEDINIPUR : Midnapur situated in the south western part of the state with a population of 3.32 million consists of plain areas with forest and forest fringes. Malaria endemicity is not uniform throughout the district and recorded API of 0.5 (SPR-1.2 SFR-0.06). Only 10% of the population is at risk of Pf malaria. Resistance study carried out in 1992 detected one RII case out of 36 cases studied. During 1997 also one RI case was detected. Resistance to chloroquine is low and focal.

CALCUTTA : The district situated on the bank of the river Ganges, having population of 50.0 million. With API 10.04 (SPR 43.0 SFR 18.1) with 48% Pf

incidence. RII and RIII level of resistance detected in 1995 in low proportion but in subsequent studies only RI level of resistance has been reported. Resistance is considered low.

S.NO.	DISTRICT	PHC	YEAR	TOTAL CASES TESTED	RI	RII	RII
1	Purulia	Ajodhya Hills	1981	50	16	4	1
			1992	31	0	3	3
			1993	37	1	5	7
			1995	31	0	5	1
			1996	34	2	0	0
			1997	30	0	2	5
2	Jalpaiguri	Dhupguri	1982	88	32	5	3
		Kamakhyaguri	1985	40	16	1	0
			1992	50	0	2	1
			1996	34	2	0	0
		Panchkolguri	1986	60	33	10	0
		Uttarlatabari	1987	32	17	2	1
			1996	32	0	0	11
		Falakata	1991	41	0	3	4
			1997	33	0	0	2
3	Calcutta	Calcutta M.Corp.	1995	43	0	1	2
			1996	33	3	0	0
4	Mednapur	Belpahari	1992	36	0	1	0
			1997	32	1	0	0

VIII. CONTAINMENT MEASURES FOR DRUG RESISTANCE FOCI

Experience has shown that there are no practical ways to eliminate chloroquine resistant *P. falciparum*, once it is well established in an endemic area. Under continued drug pressure higher degrees of resistance is likely to occur in the same area. The resistance gradually spreads to the nearby areas and also to some distant through population migration carrying resistant parasites.

In attempt to contain the spread of Pf. drug resistance, priorities were given to highly malarious areas with predominance of Pf.

In such areas due emphasis is given for carrying out containment measures. Intensification of surveillance is done for early detection & prompt treatment of cases including radical treatment. Follow up of cases is carried out. The concerted effort is made for carrying out appropriate vector control measures. Attention has also been paid for monitoring of population movement for taking effective measures for prevention of dissemination of resistant strain from area to area.

In the light of experience in neighboring countries where the resistance to many antimalarials including mefloquine has surfaced, in our country attempts has been made to prevent indiscriminate use of antimalarials by implementing NMEP drug policy chloroquine is still the drug of choice and is effective in terminating the infection in most of the areas. Second line of treatment is being followed in selective areas.

As to contain the resistant focus the following measures are recommended for strict implementation:-

1. All concerned particularly those dealing with Medical care should be aware about the situation prevailing in the area.

2. Intensive I.E.C. activities for the Health personnel and the General Public to promote sound knowledge, correct use of antimalarials.

3. A change in drug policy should however be considered only when the resistance level have reached RII and RIII degree in particular area otherwise chloroquine will still remain the drug of choice for treatment in association with primaquine.

4. Areas where isolated cases of high degree resistant foci are detected and which do not qualify for change of drug policy as per the criteria fixed alternate drugs i.e. Sulfa-Pyremethamine combination drugs should be available for second line treatment in cases not responding to chloroquine.

5. Referral centres should be capable of making correct clinical diagnosis and parasitological confirmation to ensure proper management of serious cases.

6. Interruption of transmission through indoor residual spray under strict supervision with appropriate insecticide.

7. Reduce man mosquito contact through personal protection methods like Impregnated bed nets.

8. Monitoring of population migration is very essential.

9. Longitudinal monitoring of resistance status in the affected areas.

IX. AREAS WHERE THE SECOND LINE OF TREATMENT IS RECOMMENDED

The conventional method of chemotherapy under NMEP prior to 1981 was comprised of mainly 600 mg (base) chloroquine as a presumptive treatment followed by 600 mg base chloroquine plus 15 mg base primaquine on 1st day and 15 mg base primaquine from 2nd to 5th day as a radical treatment irrespective of the species of plasmodium.

On the basis of series of In-vivo studies conducted in the country national drug policy was formulated for the first time during 1982. Areas wherever significant proportion of resistant cases were detected drug policy was revised. List of the areas are as follows :

LIST OF AREAS WITH REVISED DRUG POLICY (1981)

STATE/ U.Ts.	DISTRICTS
1. Assam	Karbi-Anglong Nowgoan
2. Arunachal Pradesh	Lohit
3. Andaman & Nicobar Islands	G. Nicobar L. Andaman
4. DNK Project	Covering areas of Madhya Pradesh and Orissa
5. Meghalaya	All districts except Jaintia Hills
6. Maharashtra	Chandrapur
7. Nagaland	All districts
8. Orissa	Keonjhar
9. Uttar Pradesh	Mirzapur

As per the drug policy 1982 Amodiaquine was administered as a presumptive treatment and sulfa-Pyrimethamine as a radical treatment in chloroquine resistant areas. In India the recent drug policy lays down that chloroquine should be used as a first line of treatment all over the country and even in areas showing RII and RIII levels of resistance. The drug schedule has been changed in selective pockets showing RII and RIII levels of resistance at 25% or above in a sample of at least 30 cases studied. In these areas, the second line of drug, i.e., Sulfa-Pyrimethamine combination has been introduced. Quinine is the drug of choice for the treatment of complicated malaria cases. However, in other areas, an individual patient who has taken complete dose of chloroquine (in the absence of vomiting and diarrhea) and not showing clinical improvement should be treated as a non-responding case and be given sulfa-pyremethamine combination. The additional areas brought under the alternate drug schedule as per the criteria are as follows.

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LIST OF ADDITIONAL AREAS BROUGHT UNDER ALTERNATIVE DRUG SCHEDULE

STATE	DISTRICT	PHC
1. Mizoram	Aizwal Lunglei	Sairang Hnahthial
2. Arunachal Pradesh	Tirap	Jairampur
3. Gujarat	Panchmahal	Kadana
4. Karnataka	Kolar	Gulur
5. Maharashtra	Raigarh	Washi
6. West Bengal	Purulia Jalpaiguri	Ajodhya Hills (Bogmundi) Uttarlatabari (Kalchini

X. CHEMOTHERAPY AND CURRENT DRUG POLICY.

The national drug policy was first drafted in 1982 to combat the increasing level of resistance to chloroquine detected in Plasmodium falciparum. Thereafter the drug policy was reviewed periodically based on the drug sensitivity studies. In the wake of recent large scale occurrence of epidemics of malaria accompanied with high mortality in different parts of the country, the question of availability of antimalarials and treatment policy of malaria cases have been debated in many quarters including the medical profession.

To look into these aspect of malaria chemotherapy, a Committee of medical experts from different specialties - clinical, pharmacology, malariology etc. - was constituted by the Dte. General of Health Services (DGHS) under his chairmanship. The Committee deliberated on various aspects of malaria chemotherapy such as (I) availability of antimalarials at national and international levels,, (ii) their pharmaco-dynamics, (iii) resistance of different species of malaria parasite to antimalarials especially P. falciparum, its distribution and magnitude of the problem in the country and (iv) response of the Indian strain of P. falciparum to different antimalarials. After extensive discussions on the information made available by the Dte. Of (NMEP), Malaria Research Centre (MRC-ICMR) and review of national international experiences along with the opinion of clinicians and pharmacologists, the Committee had observed that:-

1. Presently the following anti-malarials are available and but their use is determined by the action of each antimalarial against a particular species of plasmodium and its stages, rapidity of action, toxicity etc.

1) Schizonticidal drugs for clinical and parasitological cure
   - Chloroquine, Amodiaquine, Quinine, Quinidine, Pyremethamine, Trimethoprim, Proguanil, Sulfonamides in combination with
   - Pyremethamine, Mefloquine, Halofantrine, Artemisinine.

2) Gametocidal and anti-relapse drugs.
   - Primaquine, 8-Aminoquinolines group, only compound having action on gametocytes and hypnozoites.

As regards action of different antimalarials on different stages of malaria parasite of different species some of the salient points which were considered are:-

1. *Chloroquine* is a vary effective and rapidly acting schizonticidal drug. The drug is lease toxic with few adverse effects. Resistance to this drug has developed in P. falciparum in some parts of the country.

2. *Amodiaquine* has similar action as chloroquine, but is more toxic. It has no advantage over chloroquine in chloroquine resistant areas due to cross-resistance and therefore is not recommended for us.

3. *Sulfa and other antifolate drugs* when combined potentiate each other's antimalarial action. They are slowly absorbed and their action on parasite is much slower than chloroquine. It is recommended for use against chloroquine resistant P.falciparum only.

4. *Quinine* is an effective schizonticidal with a short half life and is used extensively - orally and in injectable form. Resistance to quinine in India has not been reported and therefore should be reserved for complicated cases.

5. *Mefloquine* - This drug is not marketed in the country but is available in the International market. It is a schizonticidal drug against all species of parasite but has not action on gametocytes and hypnozoites. It is very slowly absorbed, action on parasite is slower than any other antimalarial available. Its half life is very long. Therefore, resistant strains are selected more quickly than any other antimalarials. It has got severe toxic effects especially neuro-toxicity and should be carefully used.

6. *Halofantrine*: Available internationally and not marketed in the country. The drug has got similar action as Mefloquine. The strains resistant to Mefloquine have shown cross-resistant to Halofantrine and vice-versa. The serious disadvantage being that absorption of Halofantrine is very erratic and even with therapeutic doses, serious complications are likely to arise in spite of careful medical supervision.

7. *Artemisinine group of drugs* : These drugs have action as schizonticidal drug, their action is quicker than other antimalarials available so far. Intravenous administration of these compounds is much safer than the intravenous administration of quinine. They are comparatively less toxic than other parenterally administered antimalarials. Oral preparations are available. The drug is not marketed in India.

The committee reviewed the profile of Pf. resistance to chloroquine in the country observed that resistance is widely scattered, but in most of the pockets magnitude and degree of resistance is not very high.

After detailed deliberations and considering the present scenario of parasite profile in the country and their resistance to available antimalarials the committee observed that:

a) Chloroquine is still the drug of choice for treatment of all malaria cases in chloroquine sensitive areas of the country irrespective of the species involved.

b) 600 mg of chloroquine adult dose (10 mg per kg bd.wt) is adequate to treat P. vivax and P. malaria infection, provided the drug has been taken as a single dose. It is ingested and not vomited.

c) For treatment of P.falciparum, although inmost parts of the country 600 mg (10 mg per kg bd.wt.) is adequate but in the areas declared resistant or where the falciparum incidence is very high and other high risk areas, a dose of 1500 mg in three divided dose 600 mg single dose on each first and second day and 300 mg on the third day (25 mg per kg.bd.wt.) over three days in divided doses) will cure most of the cases P.falciparum. However, some cases may not respond, they can be presumed to be infected with chloroquine resistant strain of P.falciparum. In these cases, Metakelfin or Fansidar can be given (three tablets as adult dose). As yet, there is no resistance to these drugs in the country.

The Committee recommended that:

I The first line of treatment is chloroquine and the second line is sulfalene/sulfadoxine pyremethamine combination. In cases resistant to these two drugs and in severe and complicated malaria quinine will be used.

II All suspected malaria cases should be presumptively administered 25 mg.kg bd.wt. of chloroquine base over 3 days with a single dose of Primaquine 0.75 mg/kg. This drug regime is to be followed up to the sub-centre level throughout the country but at present to be limited to the high risk areas. In the low risk present to be limited to the high risk areas. In the low risk areas and Drug Distribution Centres (DDC) and Fever Treatment Depots (FTD) in all areas would continue to provide presumptive treatment with 10 mg;kg bd.wt. chloroquine single dose.

III The dose of Primaquine for P. vivax cases is 0.25 mg/kg daily for 5 days to prevent relapse and for P.falciparum 0.75 mg/kg single dose for gametocidal action. Where presumptive treatment with primaquine has been given in sensitive areas a second dose with it will not be required.

IV Amodiaquine has not advantage over chloroquine in chloroquine resistant areas and considering the toxicity associated with it, amodiaquine may be withdrawn from the programme and also from the private sector.

Presumptive Treatment Of All Suspected/Clinical Malaria Cases In High Risk Areas.

Chloroquine base	Day 1 10 mg/kg	600 mg adult
Primaquine	Day 1 0.75mg/kg	45 mg adult
Chloroquine	Day 2 10 mg/kg	600 mg adult
Chloroquine	Day 3 5 mg/kg	300 mg adult

Radical Treatment After Microscopic Confirmation Of Species:

P. vivax	Primaquine 0.25 mg/kg daily for 5 days
P.falciparum	No further treatment required.

In Chloroquine Resistant P. falciparum Areas:

P.falciparum - Single dose of 25 mg/kg Sulfalene/ Sulfadoxine and 1.25 mg/kg pyremethamine (3 tab.adult) with Primaquine 0.75 mg/kg

Presumptive Treatment In Low Risk Areas

Chloroquine base Day 1 10 mg/kg (600 mg adult)

Radical Treatment After Confirmation Of Species

Chloroquine sensitive areas:

P. vivax - Chloroquine 10 mg/kg single dose and

Primaquine 0.25 mg /kg daily for 5 days

P.falciparum Chloroquine 10 mg/kg plus

Primaquine 0.75 mg.kg single dose

V In severe and complicated malaria cases with P.falciparum infection (microscopically confirmed, intravenous quinine is the drug of choice,. Intra-muscular or intravenous chloroquine is not well tolerated by children and only when quinine is not available.

VI Although P.falciparum cases can be cured with the above drugs provided the treatment is not delayed and supportive therapy is started in time, the committee was of the considered view that in the light of the demand made by the medical fraternity, Mefloquine can be used for treatment of P.falciparum cases resistant to chloroquine only and not for treatment of P. vivax cases. Therefore, it is recommended that the Drugs Controller of India may stipulate strict condition for import, sale and use of mefloquine through a depot system where:

a) It should be mandatory that the drug is issued only on the prescription by a qualified registered medical specialist.

b) The prescription should be accompanied with laboratory report issued by qualified parasitologist indicating that there are P.falciparum rings in the peripheral blood and not gametocytes alone.

VII Considering the erratic absorption of Halofantrine, its toxic effect even with therapeutic doses and difficulty in management of cases with toxic manifestations,, the committee is of the opinion that this drug should not be introduced in the country. Another further corroborative factor was that Pf

resistant strains to mefloquine show cross-resistance to Halofantrine and vise versa.

VIII The Committee observed that sufficient quantity of quinine injectable is not available in the country to treat the estimated serious cases likely to occur in future. Therefore, the committee was of the view that Artemisinine and its derivatives should be introduced in the management of severe and complicated P.falciparum infection in areas of resistance foci. The drugs should be made available in injectable forms only to prevent misuse but again careful monitoring of the distribution system is imperative.

IX Quinine will be reserved for use in severe and complicated malaria but will be used in cases not responding to chloroquine and sulfa-pyremethamine combination. In case of non-availability of quinine, quinidine may be used strict cardiac monitoring.

X Primaquine is the only drug available which acts against the gametocytes of P.falciparum as well as hypnozoites of P. vivax. The Committee felt that this drug should be made available freely in the market on prescription of a physician for radical treatment.

XI Under the National Anti-malaria Programme, it is recommended that primaquine may be administered to P. vivax cases to prevent relapse for 5 days with 0.25 mg/kg daily. A 14 days radical treatment is not advocated because of toxicity, operational feasibility and also since it has very little advantage over 5 days radical treatment in an endemic area. However, those physicians who want to administer 14 days radical treatment should do so under close supervision and carefully monitor the complication which are sometime very serious with fair risk of mortality.

XII Chemoprophylaxis: The Committee was of the considered view that population living in non-endemic areas do not require Chemoprophylaxis unless they temporarily migrate to endemic areas. The population living in endemic areas except pregnant women should not be put on long term prophylaxis on account of chronic toxic effect of the drugs.

Pregnant women living in endemic and hyper-endemic areas are highly vulnerable to complications of P.falciparum because of suppressed immunity. Chemoprophylaxis is therefore recommended and should commence at the end of first trimester of pregnancy.

Travelers including service personnel who temporarily go on duty to meso-endemic or hyper-endemic areas are at high risk and therefore must be on chemoprophylaxis starting before the transmission period and terminating 4 weeks after the transmission period is over.

The temporary labour population migrating from other parts of the country to meso-endemic and hyper-endemic areas are also at high risk and should be under chemoprophylaxis. Considering that there is poor compliance from this group, the committee suggested that after initial screening and radical treatment at the point of entry, it is better to put them under weekly case detection and treatment on technical grounds.

The committee then considered the suitability of different antimalarials available for chemoprophylaxis and recommended that chloroquine is the drug of choice for chemoprophylaxis. After a loading dose of 10 mg/ kg it should be followed by a weekly dose of 5 mg/kg. This is to continue till 1 month after delivery in case of pregnancy or stay in an endemic area. Chemoprophylaxis with chloroquine because of its cumulative toxicity is not recommended beyond 3 years. In chloroquine resistant areas chemoprophylaxis is recommended with chloroquine 5 mg/kg weekly and proguanil 100mg daily.

Amodiaquine and sulfa-pyremethamine combination is not recommended for prophylaxis due to their toxic effects on prolonged use.

Mefloquine and Halofantrine were not considered suitable for chemoprophylaxis due to their toxic and also since P. falciparum resistance problem is not very serious in the country.

Quinine and Artemisinin group of drugs are not suitable on account of very short half life and consequent requirements of repeated administration of drugs.

XIII The committee deliberated on the use of Ayurvedic and Homeopathic preparations for treatment of malaria In the Ayurvedic system, Ayush-64 and other similar combination have been found to be effective against the human plasmodium. However, their treatment regimen is prolonged and has not advantage over chloroquine/sulfa pyremethamine combination. Also several homeopathy drugs are reported to be effective against malaria but need to be scientifically investigated. The committee strongly recommends that modern chemotherapeutic antimalarials are never be used in combination with Ayurvedic or homeopathic drugs because their compatibility with such drugs have been investigated so far.

XIV Monitoring of drug resistance clinically and parasitologically should also be conducted by the State Governments and the existing P.falciparum monitoring teams of NMEP would be responsible for independent monitoring in selected areas. Monitoring staff would be trained by NMEP/MRC.

XV Research institutions and Medical colleges should be involved in the development in malaria diagnostics, newer drugs, parasite sensitivity etc,. So that the National programme is updated with new technologies incorporated.

XVI To facilitate easy availability and overcome the problems of antimalarial shortage it is recommended that the Govt. Of India should develop and promote drug availability in remote areas through the private sector. The State govts. Should also establish a system to monitor availability of drugs in the periphery.

XVII Quality control of drugs should be organized and strictly implemented to ensure proper distribution of standard drugs. The State health authorities will be requested by NMEP to do sample check for drugs supplied through State Drug Controller.

XVIII Govt. Of India should initiate steps to encourage indigenous production of Cinchona and Artemesia annua. An inter-ministerial group may be set up to suggest measures for plantation in the public sector and private sector.

XIX Health education on the prevention and treatment of malaria should be a part of NMEP activities. Active involvement of CHEB should also be ensured. It is essential that wide publicity given to the revised antimalarial drug policy and to educate the medical and paramedical professionals in the private and public sectors through IMA.

XX All antimalarial drug packaging should carry full information in English, Hindi Regional languages on the dosage, side effects, antidotes, date of manufacture and expiry and other information such as on chloroquine package that ' for complete cure Primaquine therapy is necessary except in Infants and pregnant women' is necessary for safe and effective therapy.

XXI The medical practitioners should follow established guidelines but in case of non response are at liberty to administer other antimalarials and in combination with antibiotics as considered best.

XXII Malaria drug policy should be reviewed at least every two years. This is imperative in the rapidly changing epidemiology of malaria, drug resistance in P.falciparum and perhaps in P. vivax, new antimalarials and availability of more information on existing drugs.